

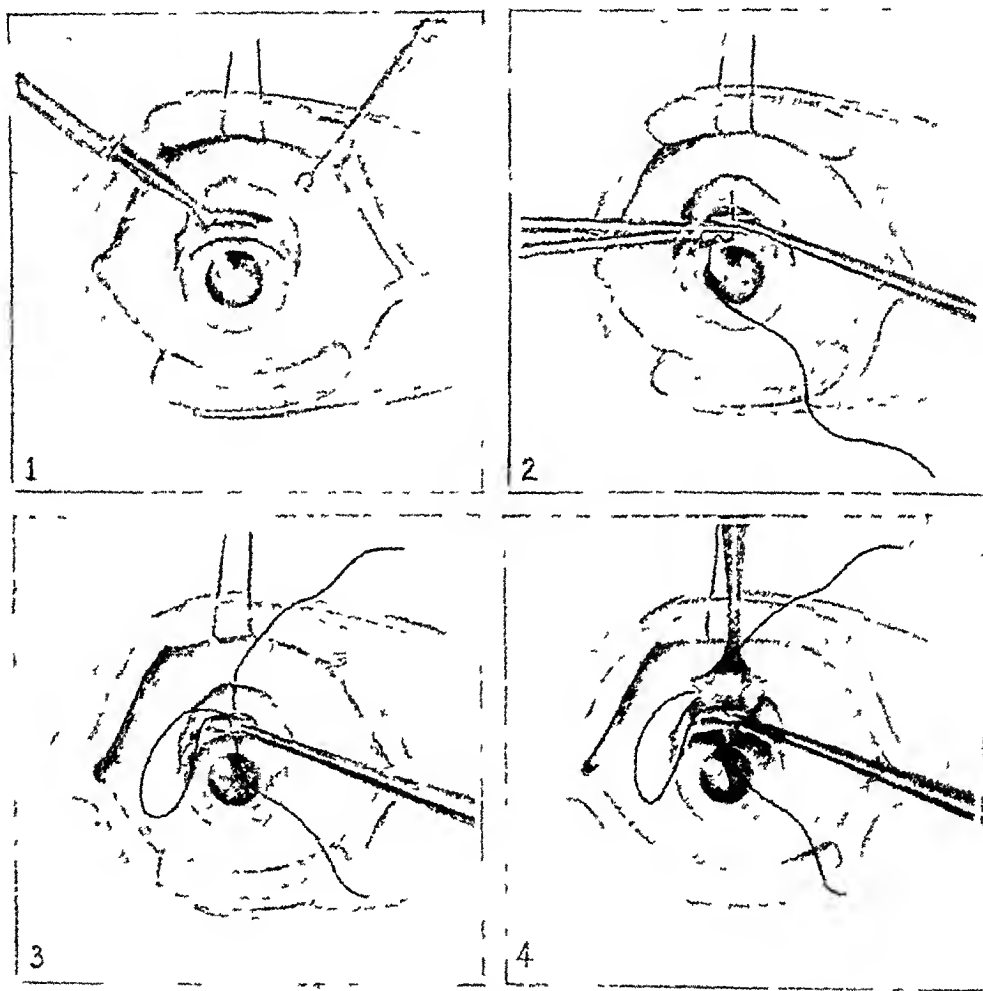


In order to overcome all these handicaps, and at the same time to afford firm and exact apposition of the lips of the wound, the technic of the scleral flap incision and scleral suture was devised, a description of which follows

Anesthesia is obtained by retrobulbar injection, and akinesia of the orbicularis oculi muscle, by the O'Brien or Van Lint injection. A retraction suture is placed through the superior rectus muscle at its insertion. This suture is left in place with no traction placed on it and is not used unless it becomes necessary, and then only with utmost care

knife being kept at a shallow level while the incision is made in order to avoid cutting through the sclera, which in this position is 0.5 mm thick. A side to side, as well as a slightly rocking, movement of the knife is used in making the incision. The knife is carried toward the limbus and stops short of opening the eyeball (fig 1)

The size of the scleral flap is more easily controlled with the concave knife than with the Lundsgaard knife. The concave knife forms a concentric, wedge-shaped scleral flap, with its base at the limbus. If the Lundsgaard knife is



Figs 1-4—1 shows the conjunctival flap dissected down over the upper half of the cornea and a concentric, wedge-shaped scleral flap being made by means of the concave scleral knife

2 shows the suture being applied through the conjunctival flap, the tip of the scleral flap and the edge of the cut scleral surface of the upper lip of the incision

3 shows the suture in place. The scleral flap has been turned down and the loop drawn aside, demonstrating the interval between the two parts of the scleral suture. The size of the interval depends on the height of the scleral flap

4 shows how the eyeball is fixed by grasping the scleral flap with a toothless conjunctival forceps. The point of the keratome has been placed in the groove at the base of the scleral flap and has entered the anterior chamber

A small conjunctival flap of about 3 mm, is dissected over the upper half of the cornea to the limbus. The eyeball is fixed with a scleral pick, and, by means of my scleral knife, which is concave anteriorly or a Lundsgaard knife, the scleral flap is made. The incision starts 1 to 1.5 mm above the limbus, the scleral

used, the edges of the flap are incised to the limbus on either side. A fine black silk suture on a sharp, curved atraumatic needle is now passed through the conjunctival flap, the tip of the scleral flap and the corresponding portion of the upper scleral lip and, finally, the edge of the bulbar conjunctiva, above. The loop is drawn

# ARCHIVES OF OPHTHALMOLOGY

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illustrates the position of the suture through the conjunctiva and the lips of the scleral wound

#### SUMMARY

It has been shown that firm and accurate closure of cataract wounds definitely reduces the incidence of postoperative complications and diminishes the amount of postoperative astigmatism. A new method for securing such closure of the cataract wound, namely, the technic of the scleral flap incision and scleral suture, is described. It permits the suture to be

taken through the lips of the wound with exactness, and the suture may be tied tightly without buckling or inversion. The scleral flap serves as an excellent point of fixation, and when it is turned downward toward the cornea, there is an ample interval between the parts of the scleral suture to permit the passage of a cataract knife or keratome without risk of severing the suture. I believe that with a little practice the occasional operator should be able readily to master the several steps of the method.

1007 Medical Arts Building





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## ENUCLEATION OF THE EYEBALL

PRACTICAL SUGGESTIONS FOR OBTAINING SATISFACTORY COSMETIC RESULTS

DANIEL B KIRBY, M D

NEW YORK

The operation of enucleation of the eyeball when performed for the relief of intractable pain in cases of absolute glaucoma or severe uveitis may elicit greater expressions of appreciation than surgical procedures which restore vision, as in cases of cataract or detachment of the retina. If, in addition, the cosmetic result in the fitting of a satisfactory prosthesis is excellent, then the happiness of the patient is more than doubled. It is possible to accomplish this. The method I have found most reliable with the least period of disability for the patient is that of simple enucleation or enucleation with immediate implantation of a hollow, nonirritating sphere, such as a gold ball, into Tenon's capsule. The newer alloys may later be found to be satisfactory substitutes for the gold. Glass has been used many times, but there is a desire for a permanent implant. I think there is no contraindication to the use of an implant even in cases of neoplasm or sympathetic ophthalmia, although it may be wise in some of these cases to do a simple enucleation and later, if desirable, to make an implantation of fat into Tenon's capsule. I should not choose to eviscerate the eyeball in cases in which there is no complication. I should, however, consider evisceration the necessary procedure in case of purulent infection of the eye because of the danger of meningitis if the optic nerve and its sheaths are cut across under such conditions.

### TECHNIC OF ENUCLEATION IN CASES WITHOUT COMPLICATION

**Anesthesia**—Local or general anesthesia may be used. In case of local anesthesia, I have used plenty of procaine hydrochloride, 2 per cent solution, to infiltrate the lids and the anterior and posterior orbital tissues, avoiding the use of more than a minimum of epinephrine hydrochloride. If general anesthesia is employed, attention to the immediate postoperative fluid balance of the

patient is important. A 5 per cent solution of dextrose in isotonic solution of sodium chloride may well be given by intravenous or hypodermic injection or rectal clysis to keep the patient from becoming dehydrated.

The operation is then carried out in five steps as follows:

**STEP 1 Incision of Conjunctiva**—The surgeon may stand at the head of the patient. The eyelids are separated with a solid-bladed speculum. The exposed lashes are trimmed. The pericorneal incision of the conjunctiva is begun at 11

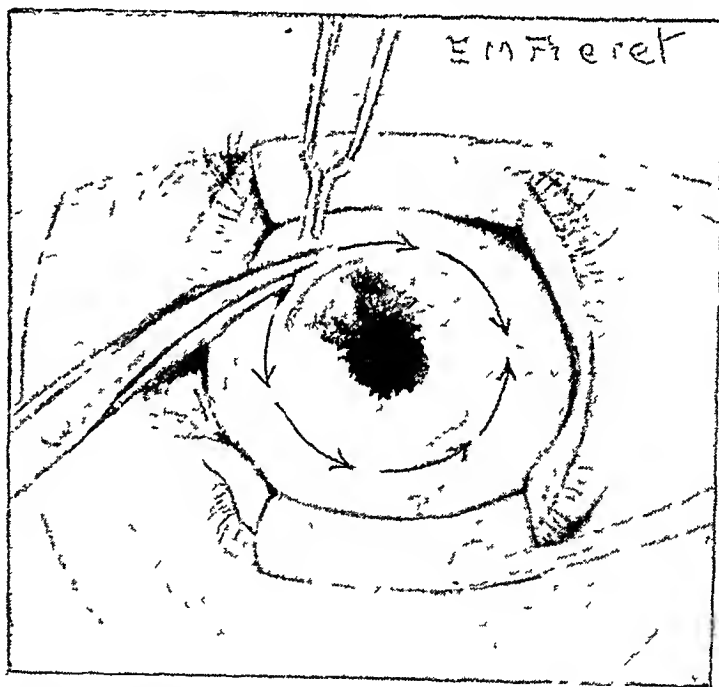


Fig 1—Incision of the conjunctiva around the corneal limbus. Note the direction of the incisions.

o'clock on the corneal dial. With undermining and cutting with curved Stevens scissors, the complete circumference is incised in three or, at most, four cuts.

**STEP 2 Section of Rectus Muscle Tendons**—Tenon's capsule is buttonholed with the same scissors inserted inferotemporally just beneath the external rectus muscle. The muscle hook is slipped carefully and accurately beneath the tendon of the muscle from below up. (It is not swept posteriorly in any uncertain fashion.) The scissors are used to sever the muscle close to its

From the Department of Ophthalmology, New York University College of Medicine and Bellevue Hospital. This paper was presented at the Forty-Ninth Annual Session of the American Academy of Ophthalmology and Otolaryngology, Chicago, Oct 11, 1944.



tendinous insertion. In the case of each muscle, the cutting with the scissors is made against the hook so that no delay will be experienced by slipping of the muscle, as may occur if done in the opposite way.<sup>1</sup>

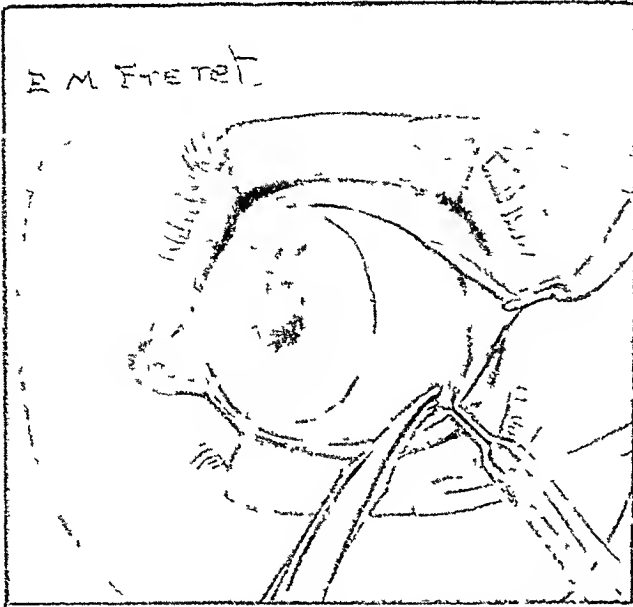


Fig 2—Incision through Tenon's capsule beneath the external rectus muscle tendon

The hook is placed beneath the tendon of the superior rectus muscle from the temporal side (to avoid the superior oblique muscle), and the superior rectus tendon is severed. I have found it easier then to proceed to the inferior rectus muscle, slipping the hook in from the temporal side, cutting the tendon, and then to the internal rectus muscle, slipping the hook up from below. In this dissection, careful observations are made for any extension of the neoplasm or for any staphylomatous protrusion in cases of trauma or perforation.

**STEP 3 Prolapse of Eyeball**—Now that the four rectus muscles have been severed, the globe may be moderately prolapsed in one of several ways, preferably, in my experience, with two small angulated scleral hooks, one under the stump of the external rectus tendon and the other under the stump of the internal rectus tendon. There is no danger of injury of the nerve posterior to the foramen if due care is exercised. This maneuver has been found to give a most satisfactory position for the next step, that of cutting the optic nerve. The globe may be prolapsed by closing

the speculum behind it or by grasping the stump of the interior rectus muscle with fixation forceps. However, the great tendency is for forceps to slip off and not to hold the globe forward.

**STEP 4 Removal of Eyeball**—Curved enucleation scissors are slipped behind the globe from the nasal side, and the optic nerve, which is placed under moderate tension by prolapse of the globe, is palpated with the blades of the closed scissors. It can easily be felt. The nasal side is chosen because the nerve runs at an angle from the apex of the orbit, which is nasalward, and can easily be straddled just behind the globe. Then the blades of the scissors are slipped backward toward the apex of the orbit, and the nerve is cut at a satisfactory distance behind the globe to avoid intraneural extension of any neoplasm or any deep cupping of the nerve head, as in case of glaucoma or posterior staphyloma. Complete removal of the globe is effected by cutting the attachments of the superior and inferior oblique muscles and of the tissue which is adherent to the globe posteriorly. If the scissors are used on the temporal side, a deeper insertion of the scissors is necessary, and the slanting course of the nerve makes for greater inaccuracy in straddling and cutting the nerve trunk. Care must be exercised not to permit the blades of the scissors to open too far, so that the ends are too far beyond the nerve, to avoid cutting through the muscle-Tenon cap-

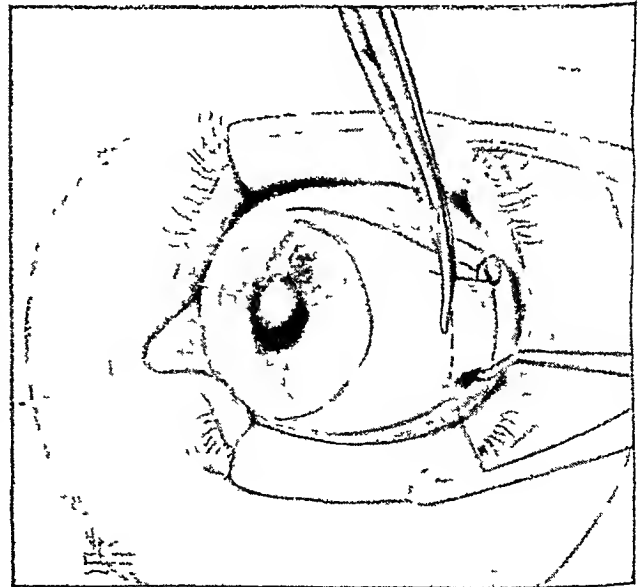


Fig 3—Severing of the external rectus muscle tendon with scissors. Note that the incision is made against the hook to prevent the muscle from slipping off.

<sup>1</sup> A silk suture for identification is placed most easily in the stump of the external rectus tendon for easier orientation by the pathologist. I have found this preferable to placing the suture in the stump of the superior rectus tendon because of the difficulty of the latter procedure in some cases, particularly with local anesthesia.

sule cone. If such an opening is made posteriorly, it may be possible for the implant to slip through and wander in the orbit.

I have tried the snare. Even with preliminary severing of the inferior and superior oblique muscles so that they will not be included in the snare, there is much tissue which is close to the posterior portion of the bulb and the nerve that is better

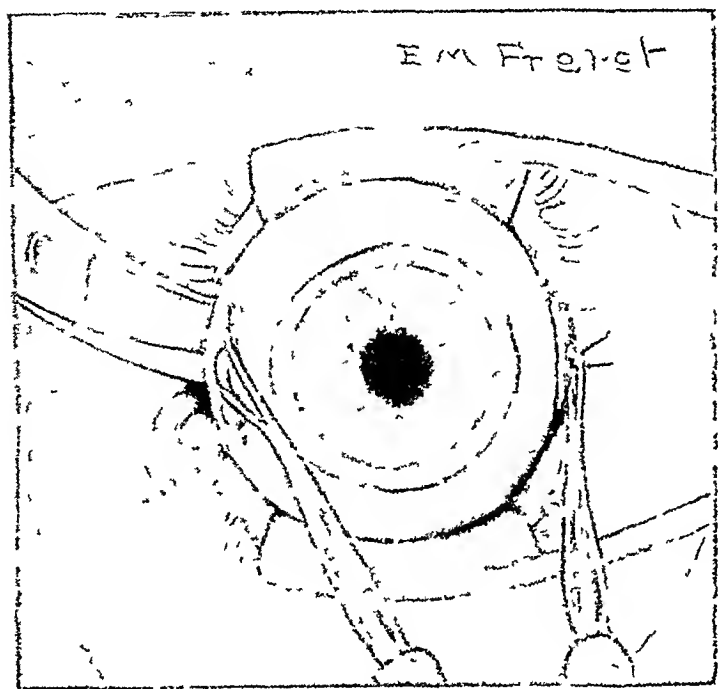


Fig 4—Prolapse of the eyeball with bipronged hooks. With enucleation scissors inserted on the nasal side of the globe, the optic nerve is more easily palpated and cut.

cut with scissors after the nerve is sectioned. Hemorrhage after cutting the nerve with scissors can be controlled and has not proved to be a serious factor. If severe hemorrhage is to occur because of the general condition of the patient, the use of the snare will not of itself control it. I have found it best not to apply severe pressure, as with an olive-tipped obturator, and not to use hot gauze packs. In other words, I avoid doing anything which interferes with the vitality and healing of orbital tissue.

**STEP 5 Closure of Incision**—In simple enucleation the incision may be closed with a simple purse string suture of the conjunctiva, or this may better be freed from the anterior portions of Tenon's capsule and later closed with a buried purse string suture of surgical gut, either plain or 0000, ten day chromic, and then the conjunctiva closed separately with interrupted sutures of plain surgical gut. There may be greater or less undesirable sinking of the orbital tissues after simple enucleation. It is desirable when feasible, to use an implantation into Tenon's capsule.

#### ✓ IMPLANTATION INTO TENON'S CAPSULE

Satisfactory results may be obtained by immediate implantation of a spherical body into Tenon's capsule. Many different shapes and

materials, organic and inorganic, have been suggested for this implantation, but the hollow-gold ball has stood the test of time. An irregular shape is no better than a smooth sphere. The size should not be over 18 mm even when an eye enlarged by disease is removed. One which is too large is apt to be worse than none at all.

#### TECHNIC OF IMPLANTATION PERFORMED IMMEDIATELY AFTER ENUCLEATION

**STEP 1 Dissection of Conjunctiva**—The globe having been removed as previously described, dissection of the conjunctiva from Tenon's capsule is performed. It should be noted that this dissection was not performed directly after the pericorneal incision of the conjunctiva. This dissection should never be done twice. Less operative trauma is experienced if the dissection is made later. It is easy enough if the assistant with two pairs of forceps holds the conjunctiva, while the surgeon with forceps on Tenon's capsule separates the two with scissors, progressing around the edge of the incision and cutting the tissues back from 6 to 7 mm.

**STEP 2 Insertion of the Sutures**—Four zero, ten day chromic gut sutures, double-armed with atraumatic needles, are used. Portions of Tenon's capsule found in the four oblique positions, between the four rectus muscles, are selected for the double-overlapping procedure, which has

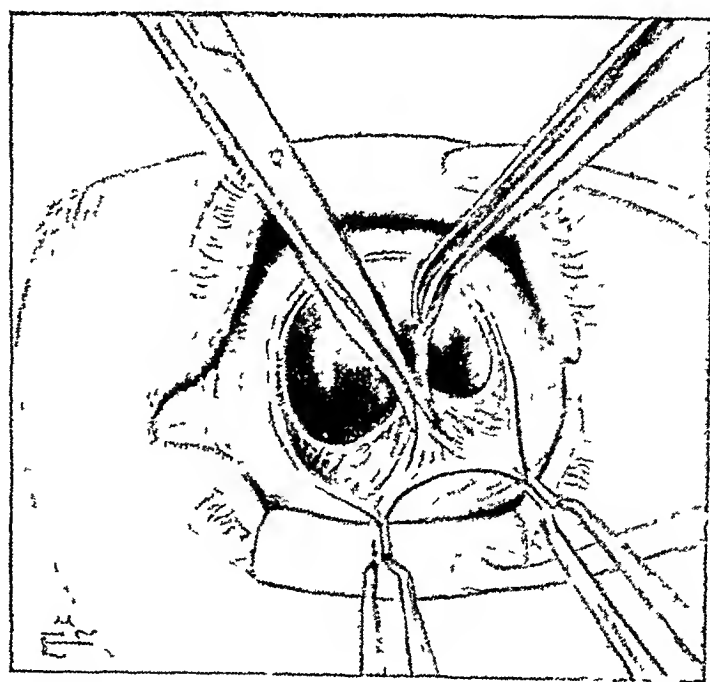


Fig 5—Dissection freeing the conjunctiva from Tenon's capsule. This is done for the entire circumference. It is best and most easily accomplished at this stage of the operation.

simply and satisfactorily served to secure the implant in Tenon's capsule-muscle cone without embarrassing the action of the muscles. The two

needles of the double-armed sutures are passed, for example, from inside Tenon's capsule out at 1 30 o'clock, then carried over and passed from within out Tenon's capsule at 7 30 o'clock. Another double-armed suture is passed in similar fashion from 10 30 to 4 30 o'clock.

**STEP 3 Insertion of the Implant**—This may be done with or without a special instrument. It is simple enough to place the sphere in Tenon's capsule-muscle cone and press it back, while the surgeon or his assistant draws up the strands of the first double-armed suture, forming a single mattress overlap of Tenon's capsule tissue, then quickly follows with the second overlap. Before the second suture is drawn secure, the first suture is tied with a square knot. The suture should be drawn firm and taut but not so tight as to cause pressure necrosis. Then the second suture is tied in similar fashion. Thus there is produced a double overlap of tissue which securely closes Tenon's capsule-muscle cone over the implant. Two muscle hooks are then used to search for openings or exposures of the implant. Usually none are found. If, however, the proper oblique positions are not chosen for the mattress sutures, an area of exposure of the sphere may require another suture but this is exceptional. The ad-

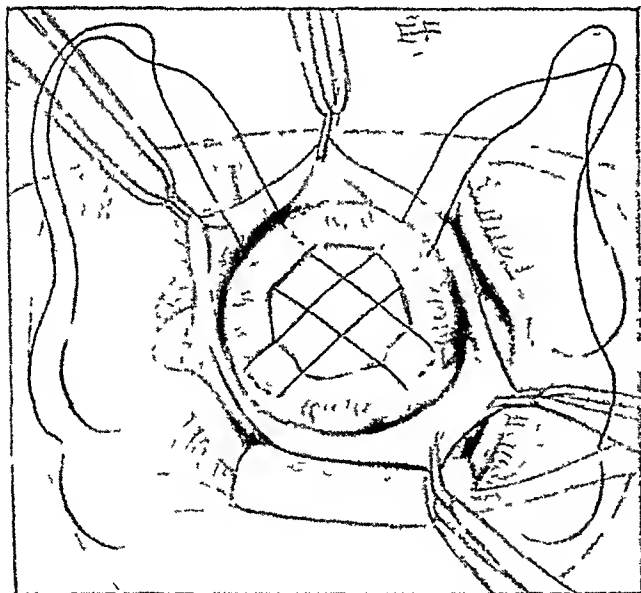


Fig 6—Insertion of 0000, ten day chromic surgical gut sutures, double-armed, from within out in diagonal positions, thus preparing for a double mattress overlap of Tenon's capsule over the implant. Note that the four rectus muscles are not included in the sutures. They retract somewhat but retain their function because of their attachments to the investing sheaths of Tenon's capsule.

Advantage of this suture technic is its simplicity, and the procedure was used with little variation by Wheeler. It does not embarrass the rectus mus-

cles in their action, as may be the effect if the sutures are placed in the muscles vertically and horizontally, drawing them too far forward. The muscles are attached firmly enough to Tenon's capsule so that they do not slip back if they are cut at their tendinous insertions. Care must be exercised not to include the tarso-orbital fascia in the sutures. This structure may be recognized

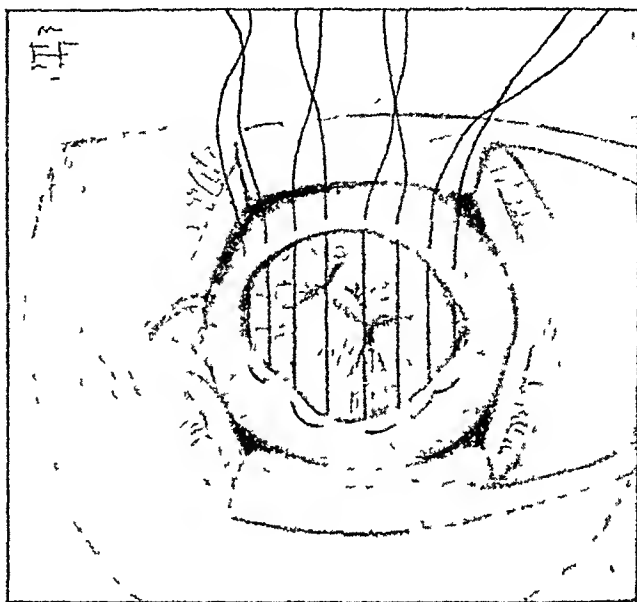


Fig 7—The double-overlapping sutures have been tied, effectively burying the implant. The mattress sutures of plain surgical gut are shown ready to close the conjunctiva.

as a white, rather dense tissue. If it is included and brought forward, considerable reduction of motility will result.

**STEP 4 Closure of the Conjunctiva**—I have found that a single-armed plain gut suture with atraumatic needle is excellent for closing the conjunctiva. A mattress suture slightly everting the conjunctiva horizontally is used in interrupted fashion. Three or four such sutures usually close the conjunctival incision efficiently. If care is not exercised in accurate appositional closure, granulations may form, which will delay healing. If such do form, they are best cut off with scissors. Caustics should be avoided.

#### DELAYED IMPLANTATION AFTER SIMPLE ENUCLEATION OR REMOVAL OF AN EYE IN A CASE WITH COMPLICATIONS

In cases in which a definite sinking of the upper lid or upper portion of the orbit develops after healing it is particularly hard to fit a satisfactory prosthesis, for an attempt by the artisan to build up the eye on top in order to fill out the depression does not achieve the desired result at

all but only spreads the lids apart and produces a decided stare. One resort in this situation is to use an implant of fat in Tenon's capsule to fill out the depression. The technic is well described in Wheeler's memorial volume,<sup>2</sup> and it is only necessary to refer the reader to it.

#### THE DRESSING AFTER ENUCLEATION WITH OR WITHOUT IMPLANTATION

It is important to provide hemostats and to prevent secondary hemorrhage and transudation by proper dressing with moderate pressure. A small amount of nonirritating antiseptic ointment or plain sterile petrolatum is placed over the closed eyelids. Then gauze fluffs are used to fill up to a slight excess the orbital depression within the bony orbital margin. Then 1 inch (2.5 cm) strips of adhesive tape are applied obliquely from the cheek to the forehead, the

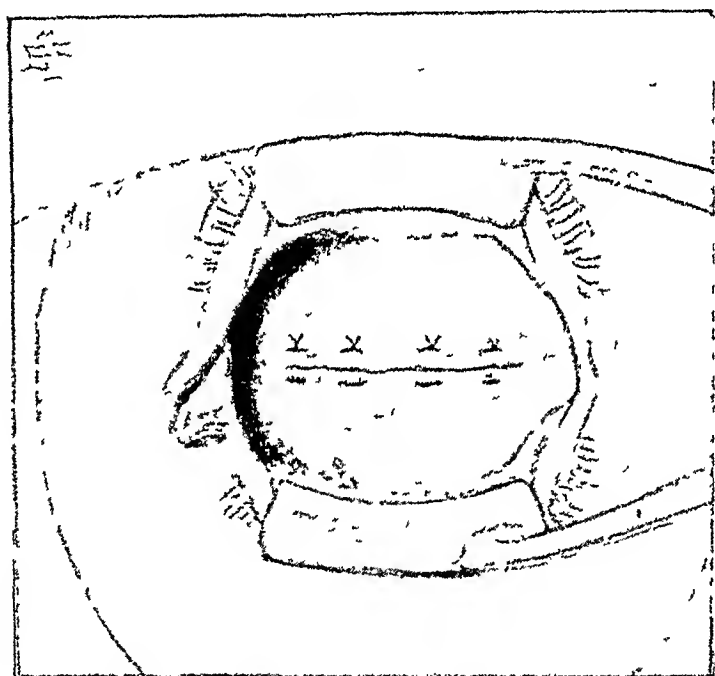


Fig 8—Closure of the conjunctiva. The implant is in the muscle cone and is covered with four layers of Tenon's capsule and conjunctiva. The socket when healed is well prepared for the prosthesis.

skin being drawn up so that the pressure will be held. After this a piece of adhesive tape is placed with sticky side out obliquely across the fellow eye, and a 2 inch (5 cm) roller bandage is applied firmly, with the turns coming up from below over the side of operation. A pad to protect the ear is excellent. The roller bandage is finally reenforced with adhesive tape. Pressure sufficient to make the dressing efficient in preventing hemorrhage is developed as the bandage is finished.

*After-Care*—The dressing is removed after five days, then is refreshed each second day until

<sup>2</sup> The Collected Papers of Dr. John M. Wheeler, New York, Columbia University Press, 1939.

the patient is ready for a temporary prosthesis. This may well be within ten days to three weeks. If complications develop, they should be taken care of according to indications.

#### THE PROSTHESIS

The prosthesis is best fitted by an expert artisan. Reform and shell eyes should be such that the artificial eye appears slightly smaller than the fellow eye. If the eye is too large, interference with motility and production of stare are common. The semilunar fold and the caruncle should not be interfered with, as they are essential for any lifelike expression of the eye.

The experienced artisan can help greatly by fashioning an individual prosthesis matching the patient's fellow eye in such respect as the color of the iris, the appearance of the sclera and the distribution of vessels.

*Care of the Prosthesis*—Any foreign body in the conjunctiva will cause secretion of mucus, and a glass artificial eye is no exception. The glass from which the prosthesis is made is porous and tends to absorb fluid and material from the conjunctiva. The surface of the prosthesis gradually erodes, roughens and becomes discolored and must be replaced. This process may be delayed somewhat by proper cleaning and polishing, which should be done regularly. The prosthesis should be removed from the socket at night. A satisfactory solution with which to cleanse the prosthesis and the socket is one slightly modified from Lancaster's formula by placing the powder in capsules as follows:

Boric acid	2.00 cc
Sodium borate	22.00 Gm
Thymol	0.15 Gm
Menthol	0.10 Gm
Oil of eucalyptus	0.40 Gm (natural oil)
Menthyl salicylate	0.40 Gm (natural oil)

Pulverize thoroughly. Divide equally into 25 capsules, of 15 grains (0.975 Gm) each. Keep reserve capsules in a tightly stoppered bottle. This powder must be freshly and individually compounded for this prescription.

Dissolve contents of 1 capsule in  $\frac{1}{2}$  pint (one ordinary tumbler) of boiling water. Bottle and use as an eye wash with an eyecup two or three times daily.

Some patients will find a solution of sodium chloride or sodium bicarbonate made with 1 teaspoon of the powder to 1 pint of sterile water more satisfactory.

#### SUBSTITUTES FOR ENUCLEATION OF THE EYEBALL

Conditions of the eye requiring enucleation usually do not permit of palliative procedures. In the face of absolute glaucoma with no vision remaining and with a sound or partially sighted fellow eye, it is unwise to hazard a procedure which may endanger the fellow eye with the pro-

duction of sympathetic ophthalmia Filtering operations, cyclodiathermy, cyclectomy and other procedures, such as opticociliary neurotomy, are not without danger in such a situation If the patient fully understands the situation, he will more readily and gracefully submit to the safer operation

In conditions of a disfigured shrunken or moderately contracted but quiet eyeball, which is free from inflammation and has been so for a reasonable time, it may be safe to denude the remains of the cornea of its epithelium and to draw over it a flap of conjunctiva for permanent covering and the fitting of a shell prosthesis If the eye is staphylomatous, this should not be done because a satisfactory appearance will not be obtained A large, protruding artificial eye will not give a good cosmetic effect

#### CASES WITH COMPLICATIONS

In cases in which extension of neoplasm has developed and is known prior to enucleation or is found at the time of the operation it may be neces-

sary to revise the plan of enucleation and proceed with evisceration of the contents of the orbit Immediate grafting of epidermis on the denuded walls and remnants of the contents of the orbit may be done, with prospects of a complete take on bone, periosteum and fat if correct apposition of the graft to the underlying bed is secured by a proper pressure dressing

If there have been extensive injury of the soft tissues of the orbit and loss of muscle, fat, fascia and production of scar tissue, the socket may need restoration in part or in full after the enucleation

#### SUMMARY AND CONCLUSIONS

My experience and technic for performing simple enucleation of the eyeball and enucleation with immediate implantation into Tenon's capsule are given in detail Relief and safety for the patient and satisfactory cosmetic results have been achieved for patients whose misfortune it is to be forced to submit to removal of the eyeball

708 Park Avenue

# PRECISIONAL ERRORS IN MEASUREMENT OF SQUINT AND PHORIA

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The purpose of this paper is to examine the degree of precision obtained with the various methods of measuring phoria and squint. It is not its purpose to suggest what degree of precision should be sought, rather, it attempts to show how far present methods may be relied on. Incorrect diagnoses of anomalies of the extraocular muscles can result from lack of attention to certain facts of geometry which profoundly influence such measurements. It is our belief that a higher degree of precision in the measurement of squint and phoria will reveal information not precisely obtainable with present methods.

Three factors comprise the errors in precision in any measurement

- 1 Inherent error in means or method
- 2 Human error in observation and manipulation
- 3 Error in degree of reproducibility, as in high precision determinations of weight or size of an object in which an average of varying results is necessary

The properties of the human mechanism are seldom constant enough to make the error in reproducibility a serious factor, hence only the inherent and the human errors will be considered.

While it is not always important to measure a single deviation with high precision, it is absolutely essential that good precision attend measurements which will be compared with one another for the purpose of diagnosis of anomalies of the various extraocular muscles. The following data, which may be expressed in any unit, illustrate the manner in which a small error may be magnified when a comparison is made between two measurements

- 1 50 with a + 10 per cent error is actually 45
- 2 40 with a 0 error is actually 40
- 3 51 with a + 2 per cent error is actually 50
- 4 47 with a 0 error is actually 47

Now, if 1 is compared with 2, the difference is 10, but with an error of 50 per cent. If 3 is compared with 1, the difference is 1, with an error of 500 per cent. If 1 is compared with 4

the difference is 3, but with an error that is wrong even in sign, for 4 is actually 2 units larger than 1, whereas even with 90 per cent precision in measurement of 1 the reverse condition appears to exist. Thus the need for a fairly high degree of precision in measurements for comparison should be apparent.

It is beyond the scope of this paper to illustrate further the theory of significant figures. The point which must generally be remembered in connection with the measurements of phoria and tropia is that a comparison of two measurements differing from each other by an amount equal to, or less than, the precisional error in those measurements is absolutely and completely without meaning and can lead to incorrect and invalid deductions. When the differences are larger than the precisional error by a small amount, the comparison has qualitative but no quantitative significance.

Squint is a manifest directional deviation from the position of a normally functioning eye. Phoria is an overcome tendency toward such a directional deviation. The direction and amount of this deviation from the position of binocular fixation are sought in measuring ocular deviations. Berlin first showed that rotation of the eye is not about a fixed point, but his and subsequent work indicates the variation from a fixed point to be so small that the error introduced by such an assumption is insignificant. All methods herein considered are based on the assumption that rotation of the eye is about a fixed point.

Four past and current means of measuring squint and phoria will be considered: (1) prisms, (2) major amblyoscopes, (3) perimeters and (4) the Hirschberg method. One new means will be analyzed, the (5) Quereau-Putnam Tropophorimeter.

## PRISMS

### INHERENT ERRORS

*Error Due to Change in Effectivity of Prisms*  
—To give a true measurement, a prism would have to be effective or perform its displacement,

at the center of rotation of the eye. Since this is impossible and the displacement of the visual line must occur outside the eye, the resulting change in effectivity is an inherent error in prism measurement. Since this change in effectivity is caused by the necessity of using the prism away from the center of rotation of the eye, it might possibly be termed a decentering error. It is of real importance in determining large degrees of squint, especially for near point measurements.

The nature of this error is diagrammatically shown in figure 1. It can be seen that the deviation of projection  $CA$  from  $FA$  is the actual angle of squint. However, ray  $FP$  must deviate from  $FA$  in order to meet the visual line and

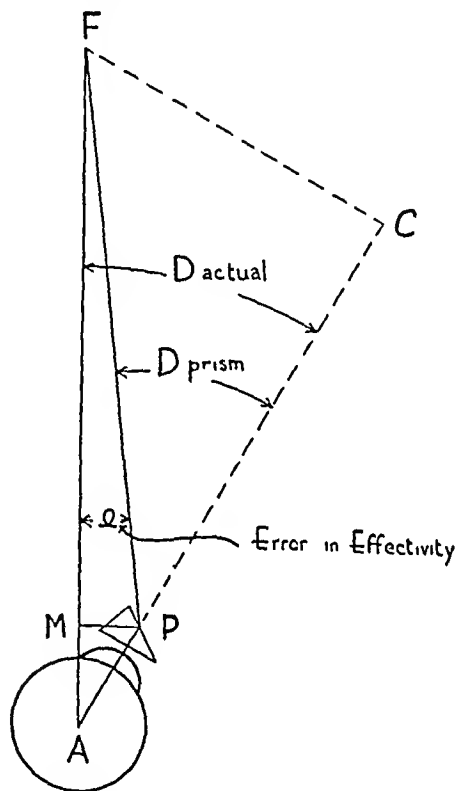


Fig 1—Diagram of error due to change in effectivity

fall on the macula. The prism measures angle  $FPC$ , which is larger than the actual angle of squint ( $FAC$ ) by angle  $e$ . This difference between the angle of actual squint and the angle of measured squint is the error due to change in effectivity. It is apparent that movement of the fixation point closer to the eye increases the error, and movement away from the eye reduces the error until at distant fixations  $FP$  is substantially parallel to  $FA$ , reducing the error to practically zero. It is further apparent that the error would increase as the prism is moved away from the eye along  $AC$  and, finally, that the greater the actual angle of squint ( $FAC$ ) the greater will be the error.

The mathematical considerations follow

$$Dp = Da - e$$

making

$$e = Dp - Da$$

Since error is the difference between the measured and the actual angle of squint,

$$e = \text{error in effectivity}$$

Consider the magnitude of this error

$$\sin Dp = \frac{FC}{FP}$$

$$\text{Hence } FC = FP \sin Dp \quad (1)$$

$$\text{Also } \sin Da = \frac{FC}{AF}$$

$$\text{Substituting (1) } \sin Da = \frac{FP \sin Dp}{AF} \quad (2)$$

$$\text{Also } \sin Da = \frac{MP}{AP}$$

$$\text{making } MP = AP \sin Da \quad (3)$$

$$\text{Substituting (2) in (3) } MP = \frac{AP \times FP \sin Dp}{AF} \quad (4)$$

$$\text{But } \sin e = \frac{MP}{FP}$$

which, from equation 4, makes

$$\sin e = \frac{AP \times FP \sin Dp}{FP \times AF} = \frac{AP \sin Dp}{AF} \quad (5)$$

While equation 5 expresses the exact size of this error, a fairly close approximation is possible, since in the angles normally measured with prisms the trigonometric sine function is nearly proportional to the angle.

Thus an approximation of equation (5) is

$$\text{error} = \text{prism-measured angle} \times \frac{AP}{AF},$$

making

$$\% \text{ error} = 100 \frac{\text{distance from center of eye to outer face of prism}}{\text{distance from center of eye to fixated object}}$$

$$\text{Actual squint} = Dp - Dp \times \% \text{ error}$$

Thus, the angle measured by a prism is always larger than the actual angle of squint, and the error is a function of the following

- 1 Measured angle of deviation
- 2 Distance of outer surface of prism from center of eye
- 3 Distance of point of fixation from center of eye

Suppose an esotropia of  $50\Delta$  is being measured by the prism and cover test with a fixation light at 13 inches (33 cm). A  $25\Delta$  prism is held base out before each eye. Suppose little attention has been given to holding the prisms as close to the eye as possible and that the distance from the center of rotation of the eye to the outer surface of the prism is 2 inches (5 cm). Applying the formula for the percentage error, the error is found to be 15 per cent, or about  $7.7\Delta$ . The esotropia for near vision, then, is actually only  $42.3\Delta$ . Further, suppose the same  $50\Delta$  measurement is made with the fixation light at 20 feet (6 meters). Applying the aforementioned formula, the error is found to be a negligible 0.8 per cent. The squint is actually greater for distance than for near vision, the primary cause probably being a divergence in-



sufficiency, but the prism measurement will not show this unless the error in prism effectivity has been accounted for. Had the prisms been held so that their outer faces were the unusually

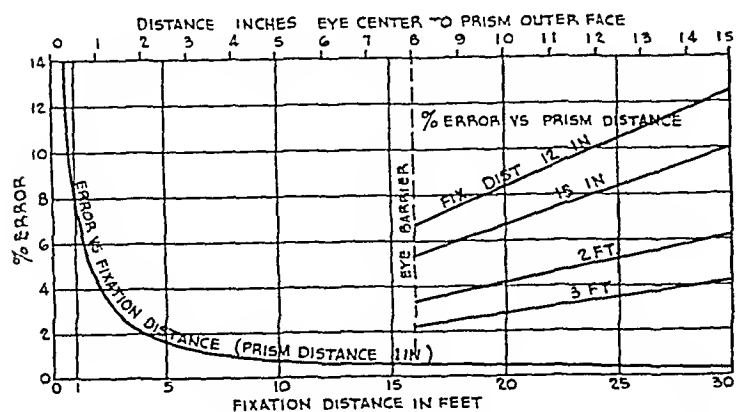


Fig 2—Percentage error due to change in prism effectivity

96 per cent. Figure 2 shows the percentage of error plotted against the fixation distance at a prism distance of 1 inch. This is an almost minimum prism distance and is well below the average normally used. The contours of the face are likely to cause increased prism distance from the center of rotation of the eye in measuring in the cardinal directions over that employed in measuring in the eyes front position. The error becomes a large factor in measuring a pronounced vertical deviation combined with a lateral tropia when a thick prism may be held base up or base down over a thick prism held base in or base out. In this case the prism distance is measured along the visual line from the center of rotation of the eye to the outer surface of the outer prism.

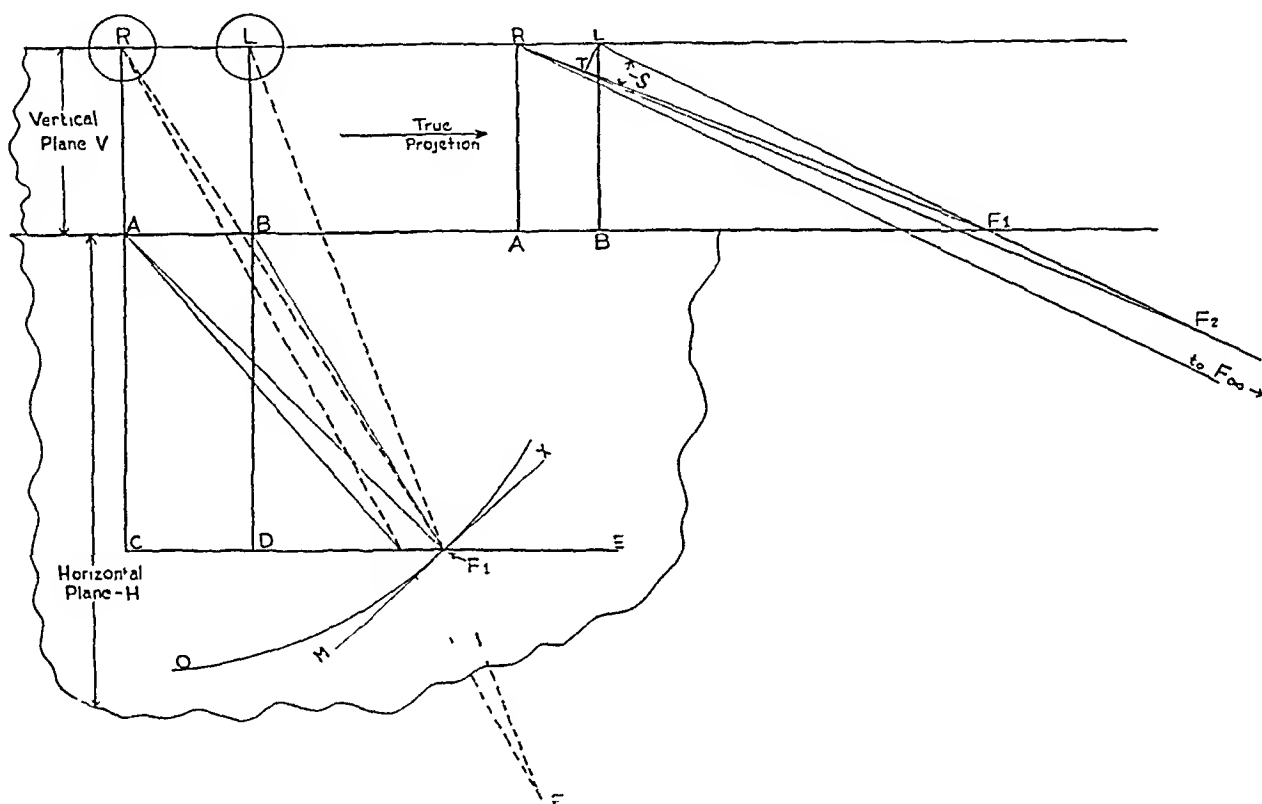


Fig 3—Diagram of oblique binocular vision

small distance of 1 inch (2.54 cm) from the center of rotation of the eye the error would have been about 7.5 per cent, or almost  $4\Delta$ . Had the fixation light in the first example been used at 16 inches (40 cm), rather than 13 inches, the error would have been  $6\frac{1}{4}\Delta$ .

Figure 2 indicates the percentage error due to change in prism effectivity showing the effect both of fixation distance and of distance from the center of rotation of the eye to the outer face of the prism at which deviation occurs when the prism is held in the Prentice position. At a fixation distance of 13 inches and a prism distance of 1 inch the error is 7.7 per cent but an increase of the prism distance by only  $\frac{1}{4}$  inch (0.64 cm) will increase the error to

*False Hyperphoria in Oblique Directions*—There is an important geometric factor concerned in measurement of vertical ocular deviations in the four oblique directions. When both eyes look down and to the left for example, in binocular fixation of a target at a near fixation distance, the visual line of the left eye is depressed a greater number of degrees below the horizontal plane than is the visual line of the right eye. The reason for this is the greater fixation distance of the right eye due to the lateral separation of the eyes. Since the target distance below the horizontal plane is common to both eyes, the difference in fixation distance necessitates different angles of depression. Near points obliquely viewed in binocular fixation require the eyes to be elevated or depressed at



different degrees above or below the horizontal, the eye nearest the target always being elevated or depressed the greater amount

This can be illustrated in an exaggerated manner by supposing that the left eye is fixing on an object straight ahead at a distance of 65 mm from the center of rotation of the eye. Further, suppose that the interpupillary distance is 65 mm. The right eye would be adducted  $45^\circ$ . Now as the fixation point is swung upward about the center of rotation of the left eye, the variation in lateral direction that existed with the eyes looking straight ahead begins to be transferred into vertical deviation, until the left eye would be elevated  $90^\circ$  but the right eye would be elevated only  $45^\circ$  above the horizontal. The geometric considerations as they concern measurement of hyperphoria and hypertropia are diagrammatically shown in figure 3.

Figure 3 is a front isometric diagram of binocular vision downward to the left. The view faces the eyes. Fixation is on  $F_1$ , which lies in horizontal plane  $H$ . The eyes are in vertical plane  $V$ . All lines lying in planes  $H$  and  $V$  are shown as solid and are in true length. Lines not in these planes are shown as lines of dashes and are not in true length. True projections, in which all lines are shown in true dimension, are shown at the right.

In binocular viewing of  $F_1$ ,  $LF_1$  is the visual line of the left eye, and  $RF_1$  is the visual line of the right eye. Right triangles  $RAF_1$  and  $LBF_1$  are in vertical planes, including the corresponding visual lines. In the true projections of these triangles, it can be seen that the angles of depression below the horizontal for the two eyes when fixing  $F_1$  are different and the difference is measured by angle  $S$ . It is also apparent that the distances from the fixation point to the two eyes differ by  $RT$ .

Now if the left eye is the fixing eye and the right eye is covered, the latter may keep the same position, but it is more probable that a small, and normal, diverging movement will occur. Near point exophorias up to  $8\Delta$  are normal. This normal exophoria results from the fact that focusing functions of an eye are not rigidly related to the convergence mechanism. Thus, the covered right eye assumes a position as though it were fixing a point farther away than the actual target but in the direction established by the fixing eye. The right eye will now have a position as though it were fixing  $F_2$ , which lies in a continuation of visual line  $LF_1$ . It can be seen in the diagram that in changing from fixation on  $F_1$  to a position equivalent to fixation on  $F_2$ , the right eye has moved not only laterally but slightly downward. The vertical

movement has in the past been either unknown or not reckoned with.

The vertical component of the diverging movement of the covered eye is shown in the true projection as angle  $F_1RF_2$ . This is a source of error in the use of the prism and Maddox rod in measurements of hyperphoria in oblique directions when normal exophoria exists. The prism or Maddox rod is normally held to give horizontal displacement and does not account for this natural vertical component of motion that occurs in the oblique directions. If abnormal lateral phoria is present, serious error is possible.

The visual line of the right eye has shifted along  $F_1C$ . The projection of the Maddox rod held so that the line appears straight and level to the patient intersects plane  $H$  along line  $MF_1X$ . This projection is above the visual line

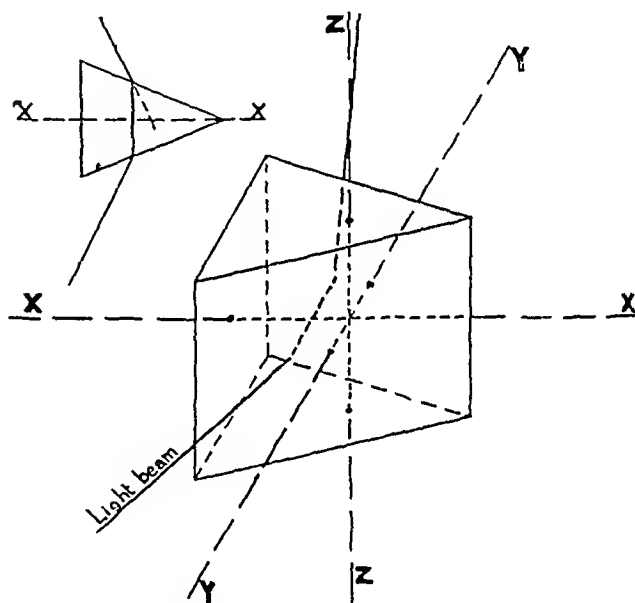


Fig 4—Axes for rotation of prism in assuming various positions used in measurement

$RF_2$ , which makes the Maddox rod appear above the target  $F_1$  as viewed with the fixing eye. An erroneous geometric left hyperphoria is thus indicated as a deviation of the ocular muscles which in fact does not exist. The Maddox rod is a continuous prism. A single prism displacing the visual line horizontally shifts the projection of the target along the same line as does the Maddox rod, resulting in the same error.

It is interesting to note at this point that if the right eye moved laterally only, and maintained the same angle of depression as in fixing  $F_1$ , the visual line would cut plane  $H$  along a circle shown as  $O$ , the center of which would be at  $A$ . The visual line of an eye depressed or elevated at any angle below or above the horizontal will describe a right cone on horizontal movement.

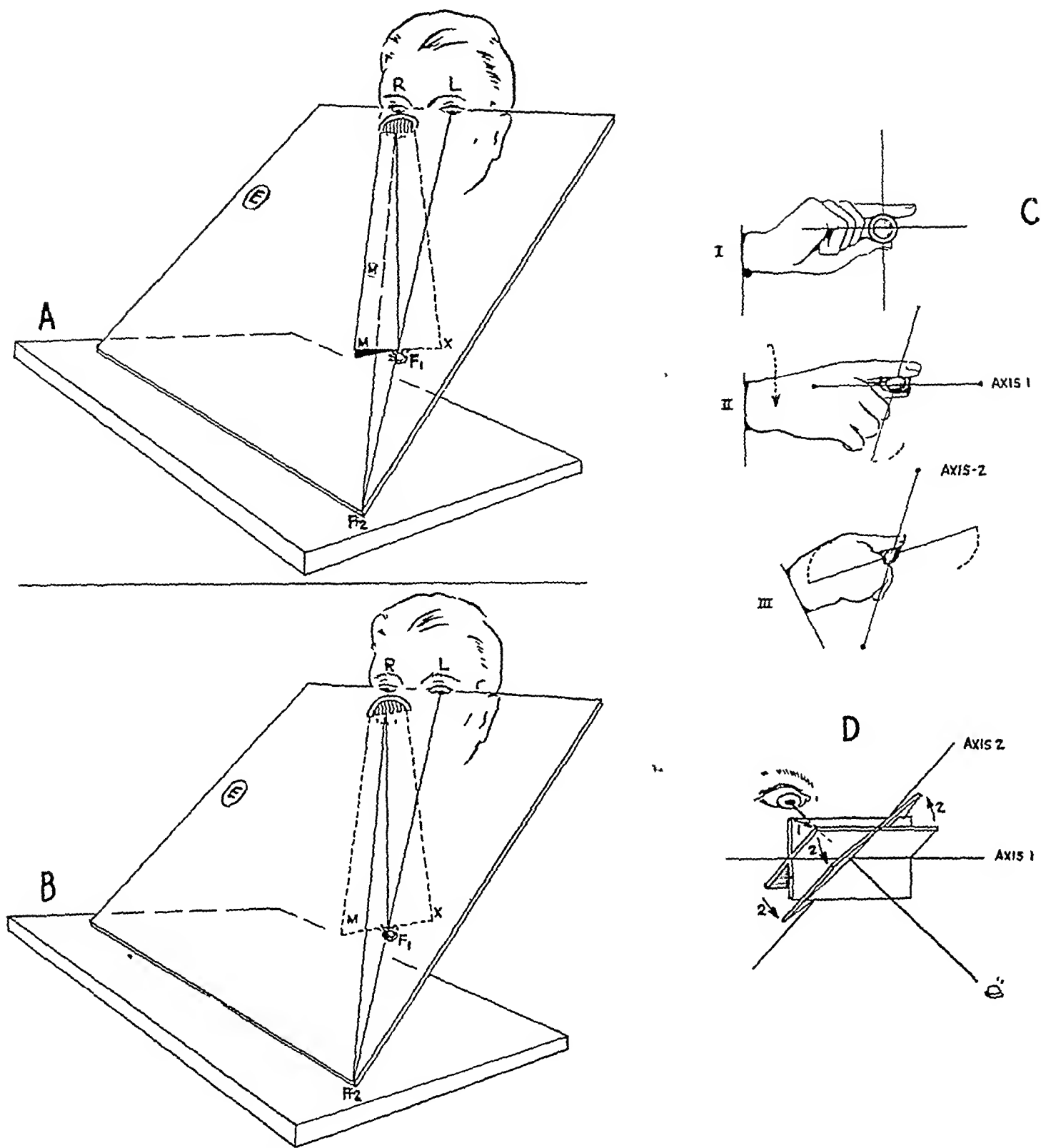


Fig 5—False hyperphoria in an oblique direction *A*, usual manner of holding prisms or the Maddox rod, in which displacement is horizontal, making the Maddox image line appear level. Light from  $F_1$  is changed by the Maddox rod to a plane which is projected outward by the eye as plane  $M$  and which is seen on edge as a level line. In oblique directions level plane  $M$  does not coincide with plane  $E$ , which contains both visual lines  $LF_1$  and  $RF_1$ . In cases of exophoria  $RF_1$  moves outward and slightly downward in plane  $E$  to  $RF_2$ . This makes Maddox line  $MF_1X$  appear above the light and results in an erroneous diagnosis of left hyperphoria, which actually does not exist. A prism held to give horizontal displacement leads to the same false diagnosis.

*B*, manner of holding prisms or the Maddox rod to avoid a mistaken diagnosis of left hyperphoria. In this position the projected Maddox plane coincides with plane  $E$  and does not appear level to the patient. When no pathologic hyperphoria exists, the right visual line  $RF_1$  will now move to  $RF_2$  along  $MF_1X$ , making the Maddox image line appear to pass through the light in cases of lateral heterophoria.

*C* and *D*, method of tilting the Maddox rod or prisms to give correct displacement in plane  $E$ . Two movements are necessary. Movement 1. From vertical position (*I*) rotate the Maddox rod about horizontal axis until it is perpendicular to plane  $E$ . Movement 2. Rotate the Maddox rod about its now tilted vertical axis until it is perpendicular to a line from the eye to the fixation light. For prisms the surface nearest the eye should be tilted as for the Maddox rod. If the first movement is about the vertical axis, the incorrect position of *A* results.

Actually, prisms can be held to shift the target along line *CE*, thus avoiding the error of a geometric hyperphoria. Rather than being displaced horizontally, the visual line should be displaced or bent in the plane of fixation, as determined by the fixation point and the centers of the two eyes. This is accomplished by keeping the *X* and *Y* axes of a prism, shown in figure 4, in the plane of fixation, as previously indicated. Likewise the Maddox rod held vertical to this plane will give the proper directional displacement to avoid error, although it will not appear level or horizontal to the patient.

Depending on the amount of exophoria present and on how far into the oblique direction the measurement is made, false hyperphoria of varying amounts will be noted, as follows:

*False Hyperphoria Present*

Direction of Near Fixation	In Exophoria	In Esophoria
Up-left	Right hyperphoria	Left hyperphoria
Up-right	Left hyperphoria	Right hyperphoria
Down-left	Left hyperphoria	Right hyperphoria
Down-right	Right hyperphoria	Left hyperphoria

It will be noted that if esophoria is present the false hyperphorias will be reversed. Obviously, when neither exophoria nor esophoria is present, there is no error. The nature of false hyperphoria can be further illustrated in a simplified manner, as in figure 5. The amount of false hyperphoria that can be measured by use of prism, Maddox rod or nearly opaque red glass can be judged from the following example:

A patient whose pupillary distance is 66 mm and whose left eye is fixing down at  $30^\circ$  and out at  $25^\circ$  on a point 15 inches (38.1 cm) distant will show a false left hyperphoria of  $2\Delta$  when an exophoria of  $8\Delta$  exists. If an abnormal exophoria of  $17\Delta$  exists, the false hyperphoria will be  $4\Delta$ . Unless the Maddox rod or prism is held so as to avoid this false hyperphoria when measuring in the cardinal oblique directions, the hyperphoria measured may be greater or less than, or even opposite in direction from, the real pathologic hyperphoria. It is interesting to note that in the example just cited binocular fixation requires the right eye to be depressed  $27.7^\circ$  (as compared with depression of the left eye of  $30^\circ$ ) and that the right eye is 16.2 inches (41.2 cm) distant from the fixing point.

*Variable Size of the Prism Diopter*—The true unit of rotational movement is the arc degree, but since employment of prisms is a common method of measuring squint and phoria the practice of using prism units (the tangent prism diopter) is rather prevalent. The prism diopter

is based on a system which makes it a constant unit of displacement, but when it is somewhat invalidly used as a unit of rotational deviation, it becomes a variable unit. This is because a unit of displacement at a larger deviation requires less angular rotation than at smaller deviations. Figure 6 shows the changing value of the prism diopter when used as a unit of rotational deviation. The value is given in terms of the arc degree which is a true unit of rotational deviation.

In the prism range of  $30\Delta$  ( $16.7^\circ$ ) the value of the prism diopter decreases from  $0.576^\circ$  to  $0.525^\circ$ , or approximately 10 per cent. Because of this ten times  $1\Delta$  is not  $10\Delta$ , nor is  $20\Delta$  added to  $20\Delta$  equal to  $40\Delta$ . An angle of  $21.8^\circ$  could be measured with one  $40\Delta$  prism or with two prisms of  $19.3\Delta$  each, totaling  $38.6\Delta$ . This results in a 3.5 per cent error. At larger angles the error becomes increasingly greater.

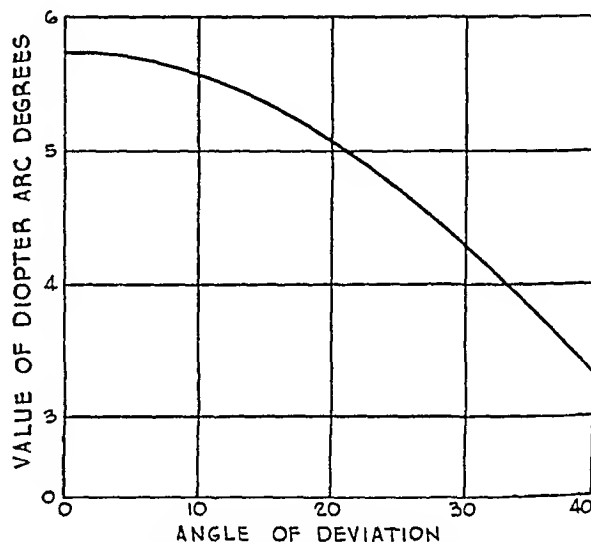


Fig 6—Value of the diopter at varying angles of deviation

Normal usage in measuring large angles is helpful. A squint measured with two  $25\Delta$  prisms is called a  $50\Delta$  squint. The angle is actually  $28.1^\circ$ , or  $53.3\Delta$ , but the practice of adding the separate measurements reduces the error resulting from the varying unit. The prism diopter is roughly 0.5 arc degree. Unless this assumption is used in determinations, it is not a source of error. The sole source of error is in the variation of the value of the prism diopter when used as a rotational unit. That such a system of measuring angular deviation of the eye is subject to inherent error is obvious. While errors of the magnitude encountered in this system are not always significant, their presence should be recognized if not actually accounted for. They are of sufficient magnitude to affect

conclusions drawn from measurements for comparison

#### HUMAN ERROR OF MANIPULATION

*Variable Prism and Target Distances*—The human error of manipulation can greatly affect the inherent error in effectivity. The distance of the prism from the eye can easily vary from one measurement to another. The size of the error and the effect of prism distance were pointed out previously. Likewise, the distance of the fixing object, such as a small light, may easily vary a few inches. In this way, the human error is again injected into the error in effectivity, to a degree previously shown in figure 2. Figure 7 is a diagrammatic illustration.

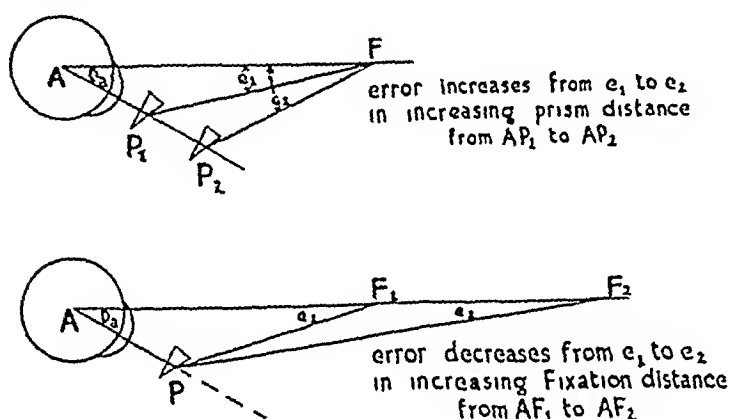


Fig 7—Variation of error in effectivity with changing prism and fixation distances

Another factor in prism measurement is the human error possible in measuring in the cardinal directions. While measurements of squint and phoria in any of the cardinal directions are in the field of action of the various ocular muscles, it is important to know how far into the field the measurement is being made if the results are to bear good quantitative significance. It is not easy to judge the exact angle of a target from the horizontal and vertical planes.

*Changes of Prism Strength with Rotation*—Still another human error in manipulation is found in the error due to variation of the prism from its theoretically proper position. Rotation about the Z axis (fig 4) is the most serious variation affecting precision. A most thorough and searching treatment of this by Dr. Le Grand Hardy<sup>1</sup> is concurrently published with this paper. It completely covers the serious errors encountered in rotation about the Z axis.

Rotation about the Y axis tends to rotate the bending plane and thus to turn horizontal bending into vertical bending. A prism held

base in or base out before the eyes can be rotated through  $5^\circ$  without appreciable effect on the lateral measurement. However, the prism is in a position to affect maximally the vertical component of bending. If a lateral correction is made prior to measuring a vertical deviation, then vertical axes pass through the centers of error in the vertical measurement. This can easily be shown by holding a Maddox rod in front of the eye horizontally. A  $20\Delta$  prism is held base in before the same eye, and, without the Maddox rod being moved, the prism is rotated slightly. Without considerable care in holding compensating prisms, error up to  $2\Delta$  can easily be injected into the measurement being made at right angles to it.

Rotation about axis X (fig 4) causes an insignificant error, although there is some effect, as can be demonstrated by viewing a vertical straight line, such as a door frame, through a prism held base in or base out. If the viewer is within 6 feet (182.8 cm) of the door, the frame will appear bowed, as the result of different angular passages through the prism as he looks from the top to the bottom of the door.

#### AMBLYOSCOPES

Measurement of tropia and phoria with any of the various modifications of the amblyoscope does not involve any inherent precisional errors. However, in practice, their vertical axes are usually placed well forward of the center of rotation of the eye in order to accommodate esotropia. Unless these axes are placed forward of the center of rotation of the eye, the reflecting mirrors or prisms interfere with one another or with the nose. This forward position of the axes introduces a decentering error, or error in effectivity, exactly in the manner previously explained with prisms. At distance fixations the error is of no consequence, but at near points of fixation this practice is the source of substantial and significant error.

The human error in observing scale readings should not be significant if they can be read to  $0.25^\circ$ , or  $\frac{1}{2}\Delta$ .

There is a source of human error on the part of the patient in measurement with amblyoscopes. The use of lenses to create an artificial fixation distance does not bring into play the psychic factors affecting the conception of distance. Thus, when the psychic sense of distance is strong, considerable variation in lateral measurements will occur, introducing precisional errors of variable, unpredictable and indeterminate magnitude.

<sup>1</sup> Hardy, LeG. Clinical Use of Ophthalmic Prisms (Metric), Arch. Ophth., this issue, p. 16

## PERIMETERS

Perimeters are primarily designed to measure the field of vision. For this reason they are almost universally made to give readings or data in the polar coordinate system, which is most desirable in perimetry. This limits the direct reading of lateral tropia to the horizontal plane and the direct reading of vertical tropia to the vertical plane directly in front of the measured eye. Aside from direct readings in these limited directions, considerable mathematical computation must be made to determine lateral and vertical tropias. This is necessary to determine vertical or lateral deviations from polar coordinate data.

No inherent errors are encountered if the nonfixing eye is kept in the center of the measuring arc to avoid a decentering error. However, considerable ingenuity is necessary in choosing target positions so that the proper reference position for the nonfixing eye is known. While the perimeter is admirably suited to measurement of the visual field, this instrument is practically useful in the measurement only of lateral tropia in the horizontal position. As the instrument is generally used, the degree of precision obtained is not sufficient to warrant deductions from comparative measurements. For instance, a comparison of measurements for near and distant fixation

## HIRSCHBERG REFLEX METHOD

The Hirschberg method is particularly useful in measuring tropias in very young children when more accurate methods are not practical. It is also useful for patients who do not have central fixation in the squinting eye and whose squint must be measured objectively.

When the squint is to be measured at the near distance, the patient fixes a light held at 33 cm in front of his fixing eye. The examiner's eye is placed behind the light and in line with it and the patient's squinting eye. The position of the light reflex on the squinting eye is then noted. Each millimeter of displacement of the light reflex from the center of the cornea of the squinting eye equals  $7^\circ$  of arc. An approximate allowance for the angle  $\kappa$  as observed in the fixing eye should be made.

If the position of the reflex can be measured by a millimeter rule, the precision of the measurement is slightly over 0.5 mm. In the case of young children who will not permit a rule to be placed in front of the eyes, the examiner must judge the distance of the reflex from the center. In this case judgment to within 1 mm is all that can be expected, and hence the preci-

sion is not better than  $7^\circ$ . When a rule can be used, the precision is about  $5^\circ$ , or certainly no better than  $4^\circ$ .

The measurement at distance fixation is the weak point in the Hirschberg method. The average convergence at near point fixation is about  $10^\circ$ . In measuring at distance fixations a new reference light position must be used, or this  $10^\circ$  becomes a source of error, causing the measurement of a convergent squint to be  $10^\circ$  less, and that of a divergent squint  $10^\circ$  more, than the actual value. To avoid this, either the distant object must be the source of light for the corneal reflection or a near light must be shifted into a line connecting the squinting eye with the distant object. It is difficult to insure proper fixation for a child at distance with the examiner's head so close to the line of fixation. The precision of the Hirschberg method at distance is not better than 7 or  $8^\circ$  of arc. Therefore, comparisons with near point values for tropia contain a precisional error of  $11^\circ$  to  $14^\circ$ .

## THE QUEREAU-PUTNAM TROPOPHOROMETER

The present understanding of the action, functions and motivations of the ocular muscles has advanced to a point which makes errors of the magnitude just mentioned a serious shortcoming in diagnosis. Efforts toward the end of reducing precisional error to a minimum in the measurement of tropia and phoria led to development of the Quereau-Putnam Tropophorometer.<sup>2</sup> This instrument is without inherent error. Its targets move spherically about each eye's center of rotation, and actual distance, both far and near, is used in fixation, instead of the illusion of distance. These features are combined in an instrument designed to be used with the cover test for the best possible elimination of the tendency toward fusion.

The human error of manipulation is present in adjusting the head and the instrument to their proper positions. With such an instrument the interpupillary distance can be adjusted to within 1 mm. Vertical adjustment can be made to within 1 mm, and forward or backward adjustment, to within 2 mm. With ordinary care maximum deviation of the sphere center from the center of rotation of the eye will not exceed 3 mm and will average under 2 mm. This is a source of decentering error too small to affect significantly any measurement even at the nearest fixation distance that may be desired, being

<sup>2</sup> Quereau, J. V., and Putnam, O. A. Quereau-Putnam Tropophorometer, *Arch Ophth* 33:28 (Jan) 1945.

under 1 per cent at a fixation distance of 12 inches (30.48 cm). Scales can be read to  $0.25^\circ$ , and the instrument affords a means of knowing precisely how far into the fields of action of the oblique and rectus muscles each measurement is made.

### CONCLUSION

A knowledge of the degree of precision and of error inherent in various methods of measuring squint and phoria discussed in this paper and of the means of compensating for them will increase the accuracy of diagnosis of anomalies of the extraocular muscles. These errors and the means of compensating for them may be summarized as follows:

1. The error in effectivity in prism measurements is the angle formed by a line from a fixation point to the center of rotation of the eye and a line from the fixation point to the outer surface of the prism at a point such that after refraction it will coincide with the visual line of the eye.

For small measurements, the error in effectivity may be sufficiently minimized by (1) holding the muscle light at least 16 inches (40.6 cm) away from the patient and (2) holding the prism as close to the eye as possible.

For large measurements ( $25\Delta$  and over), the error in effectivity may be compensated for by subtracting the error in effectivity from the measured deviation in which

$$\% \text{ error} = 100 \frac{\text{distance from center of eye to outer face of prism}}{\text{distance from center of eye to fixated object}}$$

2. False hyperphoria in the oblique directions is measured when either exophoria or esophoria exists and the measurement is made at near fixation distance.

(a) For prisms, the error in diagnosis due to false hyperphoria can be avoided by (1) rotating the laterally measuring prism slightly around its horizontal axis ( $X$ , fig. 4) until its near (inner) surface is perpendicular to the plane of fixation (movement 1, fig. 5 *C* and *D*), then (2) rotating the tilted prism around its vertical axis ( $Z$ , fig. 4) until the near surface is per-

pendicular to the portion of the visual line from eye to prism (movement 2, fig. 5 *C* and *D*).

(b) The Maddox rod should be tilted exactly as for the near surface of a prism which is correcting the lateral deviation, as previously described. When this is done, the line formed by the Maddox rod will not appear horizontal (or level) to the patient. The patient will see the line tilted so that its nasal end is lower than the temporal end when measurements are made below the horizontal plane, and its nasal end is higher than the temporal end when measurements are made above the horizontal plane.

(c) The red glass cannot be held so as to compensate for the false hyperphoria in oblique directions. It can be used accurately only when no esophoria or exophoria exists, for then there will be no false hyperphoria. The red glass has accuracy in the horizontal and vertical planes but not in the oblique directions.

3. Variations in the size of the prism diopter unit need not be considered a serious source of error. This is because the practice of employing two prisms of moderate size and adding their dioptric power, instead of using one very strong prism, effectively minimizes the error due to the variation in the value of the prism diopter unit, which is serious only in large prisms.

4. Variation in prism and target distance from one examination to another is a source of error unless a record is kept of the distances used and these distances are kept constant.

5. Change of prism strength with rotation may be minimized by strict observance of the Prentice position or by eiring on the side of the split position.<sup>1</sup>

6. Amblyoscopes have a large decentering error when set for near point measurement unless their vertical axes pass through the centers of rotation of the eyes.

7. Perimeters and the Hirschberg reflex method are useful only for gross measurement of lateral tropia.

Dr. LeGrand H. Hardy made helpful suggestions and corrections in the preparation of this manuscript.

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# CLINICAL USE OF OPHTHALMIC PRISMS (METRIC)

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In a previous report<sup>1</sup> the origins and developments of the present systems of numbering ophthalmic prisms were discussed, and attention was called to three important facts

- 1 The power of prisms frequently departs unjustifiably from reasonable manufacturing standards
- 2 Different units of power are used, but the unit used is rarely indicated on the label
- 3 Enormous errors are introduced in using strong prisms unless careful precautions are taken respecting the position in which the prism is held and the unit used

Both the Dennett<sup>2</sup> system of utilizing the prism centrad ( $\nabla$ ) as a unit and the Prentice system<sup>3</sup> of utilizing the prism diopter ( $\Delta$ ) as a unit require that all refractive effect must take place at one surface. This condition is violated more frequently than it is observed in clinical practice. I have watched many ophthalmologists, teachers as well as students, in making their measurements of squint, and the usual procedure is to hold the prism between thumb and forefinger in such a position that the altitude of the prism is roughly in line with the forefinger, and it is this line which is held approximately normal, or at right angles, to the optic axis of the deviating eye (X axis, fig 10)

To simplify the discussion, I shall call this position the "split position" (the visual line of the eye is normal to a line splitting the apex angle of the prism), and the purpose of this discussion is to analyze the errors introduced into measurements by improper positioning of the metric prism

Accepting for the moment the prism diopter as the operational unit of strength of the prism and ignoring the Prentice postulate that all effect must take place at one refractive surface, one may consider how deviations from this position affect the apparent power of the prism

From the Knapp Memorial Laboratories, Institute of Ophthalmology, Presbyterian Hospital

1 Hardy, L. H., Chace, R. R., and Wheeler, M. Ophthalmic Prisms: Corrective and Metric, Arch Ophth 33:381 (May) 1945

2 Dennett, W. S. A New Method of Numbering Prisms, Tr Am Ophth Soc 5:422, 1889

3 Prentice, C. F. A Metric System of Numbering and Measuring Prisms, Arch Ophth 19:64 and 128, 1890

Seven fixed positions immediately become apparent

- 1 The position of maximal deviation ( $e = 90^\circ$ ), in which the emergent ray just grazes the surface of the prism
- 2 The position of the maximal deviation ( $i = 90^\circ$ ), corresponding to position 1, in which the entering ray just grazes the surface
- 3 The position of minimal deviation, in which the prism exerts its least effect. In this position the ray inside the prism travels at right angles to a line bisecting the apex angle, i. e., in a symmetric prism the ray inside travels parallel to the base ( $e = i$ )
- 4 The Prentice position, in which the entering ray meets the first surface of the prism at right angles ( $i = 0^\circ$ )
- 5 The Prentice position, corresponding to position 4, in which the path of the ray is reversed. In this position the emerging ray is perpendicular to the last surface ( $e = 0^\circ$ )
- 6 The "split position," in which the entering ray outside the prism is traveling on a line at right angles to the line bisecting the apex angle. This is the position in which prisms are usually observed to be held ( $i = \frac{a}{2}$ )
- 7 The reverse of the split position, in which  $e = -\frac{a}{2}$

Measurements of twenty sets of prisms were made in all these positions and checked against calculated values, to produce the accompanying charts and table

The following formulas were derived for the powers of deviation ( $\delta$ ) of various prisms held in these positions. All formulas were derived directly from Snell's law ( $n \sin i = n' \sin r$ ), using the index of refraction of glass as  $n' = 1.523$ . This index, by reverse calculation was made a basis for checking on the accuracy of measurements

The formula for maximal deviation ( $\delta_{max}$ ) is

$$\delta_{max} = \sin^{-1} n' \sin (a - C) + 90 - a \quad (1)$$

The formula for minimal deviation ( $\delta_{min}$ ) is

$$\delta_{min} = 2 [\sin^{-1} (n' \sin \frac{a}{2})] - a \quad (2)$$







the split position is much less aberrant, but it, too, follows the inevitable course, and all curves reach a common point (at  $\alpha = 81^{\circ} 32'$ ) where the deviation becomes infinity

How does the deviation vary with respect to the position, that is, to the angle of incidence? It has been found possible to develop a formula for this,<sup>4</sup> which is

$$\delta = \cos^{-1} \left[ \left[ n' \cos \left[ \alpha + \cos^{-1} \left\{ \frac{\cos (90 - i)}{n'} \right\} \right] \right] \right] - (90 - i + \alpha) \tag{9}$$

Apex Angle ( $\alpha$ ) for Prisms 1  $\Delta$  to 115  $\Delta$  Calculated \*

Apex Angle ( $\alpha$ )		Prism ( $\Delta$ )
Degree ( $^{\circ}$ )	Min ( $'$ )	
1	06	1
2	11	2
3	17	3
4	21	4
5	29	5
6	31	6
7	35	7
8	36	8
9	40	9
10	41	10
11	42	11
12	39	12
13	38	13
14	35	14
15	32	15
16	25	16
17	20	17
18	11	18
19	01	19
19	54	20
23	40	25
26	58	30
29	42	35
31	58	40
33	53	45
35	26	50
37	42	60
39	09	70
40	06	80
40	37	90
40	55	100
41	01	110
41	02	115

\* This table illustrates the commonly taught fact that there is little difference between the apex angles, in degrees, and the dioptric strength, in prism diopters up to about 20  $\Delta$ , but that beyond this point the difference increases with great rapidity

Since the critical angle for glass with an index of refraction ( $n'$ ) of 1.523 is  $41^{\circ} 02'$  in apex angle of this dimension represents the strongest that can be manufactured and marked in prism diopters

If one ignores the Prentice position, the strongest possible prism would have double the critical angle of glass as its apex angle, it would deviate a ray of light through more than a right angle ( $97^{\circ} 56'$ ) and would hence have what might be considered as a minus power of  $-717.6 \Delta$

From this formula has been calculated a family of curves (one curve for each prism) showing the apparent effect produced as the prism was rotated from the position at which  $i = 90^{\circ}$  to the position at which  $e = 90^{\circ}$ . Since the concepts considered here are predominantly concerned with prism diopters, the values for  $\delta$  (given in the formula as degrees, or  $\delta^{\circ}$ ) have been transformed (invalidly) into prism diopters ( $\delta \Delta$ )

$$\delta \Delta = 100 \tan \delta^{\circ} \tag{10}$$

The index of refraction of glass is considered throughout as  $n' = 1.523$ . The value for  $i$  is assigned. The value for  $\alpha$  is taken from the table. The value of  $\delta$ , expressed in degrees ( $\delta^{\circ}$ ), is calculated and converted into prism diopters ( $\delta \Delta$ ) by formula 10

The results are arresting and instructive. They can better be seen in graph form than in a table, since fifteen pages of tabular material can be presented in one graph. Figure 9 presents the data derived from the foregoing calculations

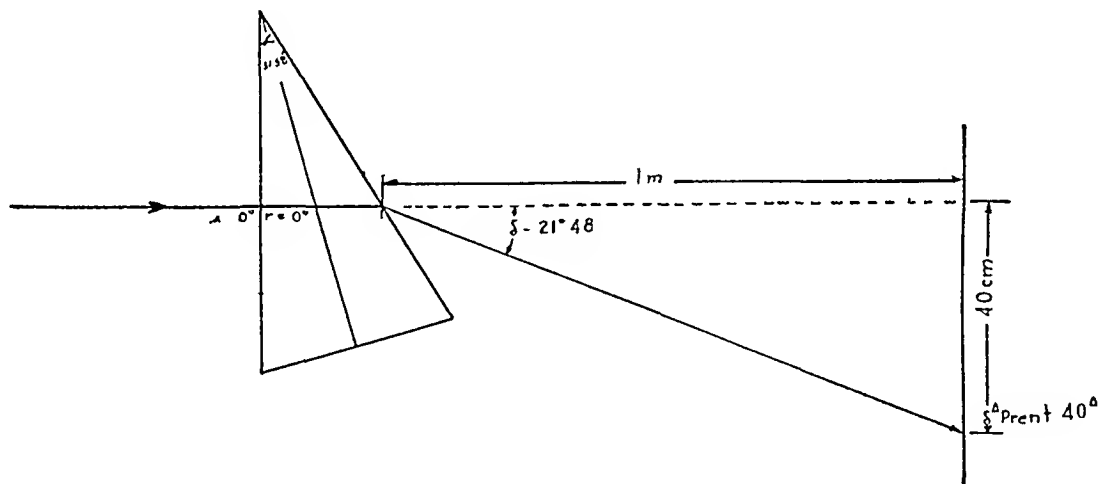


Fig 2—Deviation produced by a 40  $\Delta$  prism of glass ( $n' = 1.523$ ) when held in the Prentice position, in which  $i = 0^{\circ}$

EFFECTS OF ROTATING MEASURING PRISMS

It is obvious that the measurements and calculations so far recorded have yielded deviations produced in seven positions which represent only points in a continuous curve. That is, the deviation produced by any prism will vary continuously from one maximum ( $i = 90^{\circ}$ ) down to the minimum deviation and back up through the deviations for the split position and the Prentice position to a second, and equal, maximum deviation, where  $e = 90^{\circ}$

Each curve represents the effects produced by a single prism. The left hand ordinate ( $i = +90^{\circ}$ ) indicates the maximal effect produced when the incident ray grazes. The heavy upward curving line represents the effect produced in the position of minimal deviation, the light similarly curving line shows the effect produced in the split position, the straight vertical dotted line at  $i = 0^{\circ}$  marks the effect produced

4 Dr Paul Boeder helped in developing this formula and checked all the other formulas

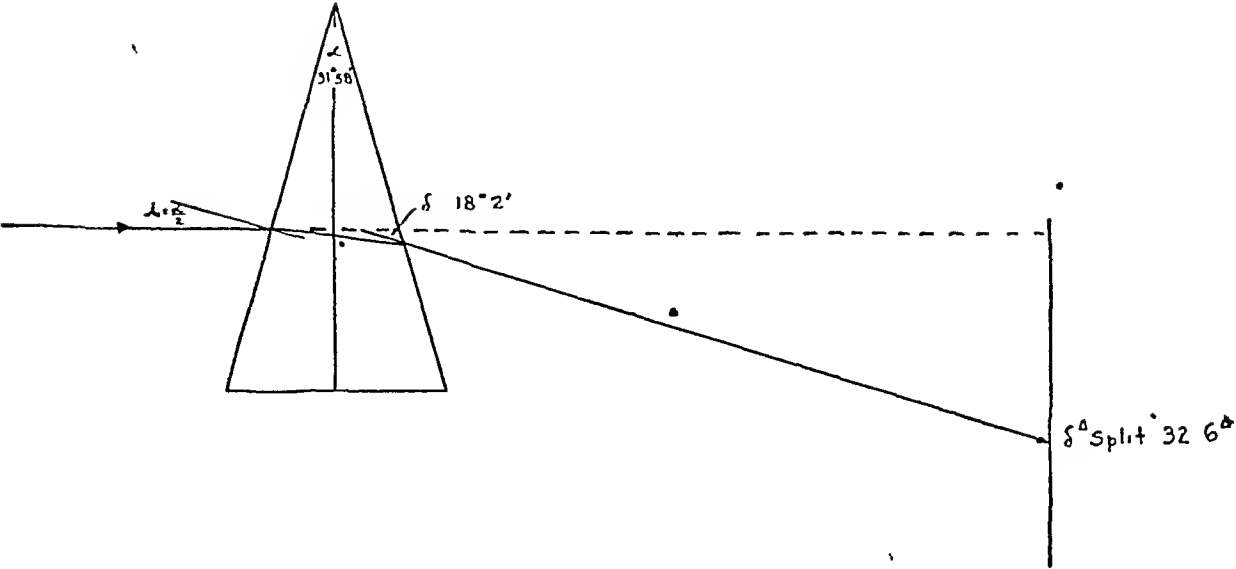


Fig 3—Deviation produced (invalidly recorded in prism diopters) by the same  $40 \Delta$  prism (apex angle,  $31^{\circ} 58'$ ) when held in the split position, in which  $i = \frac{a}{2}$

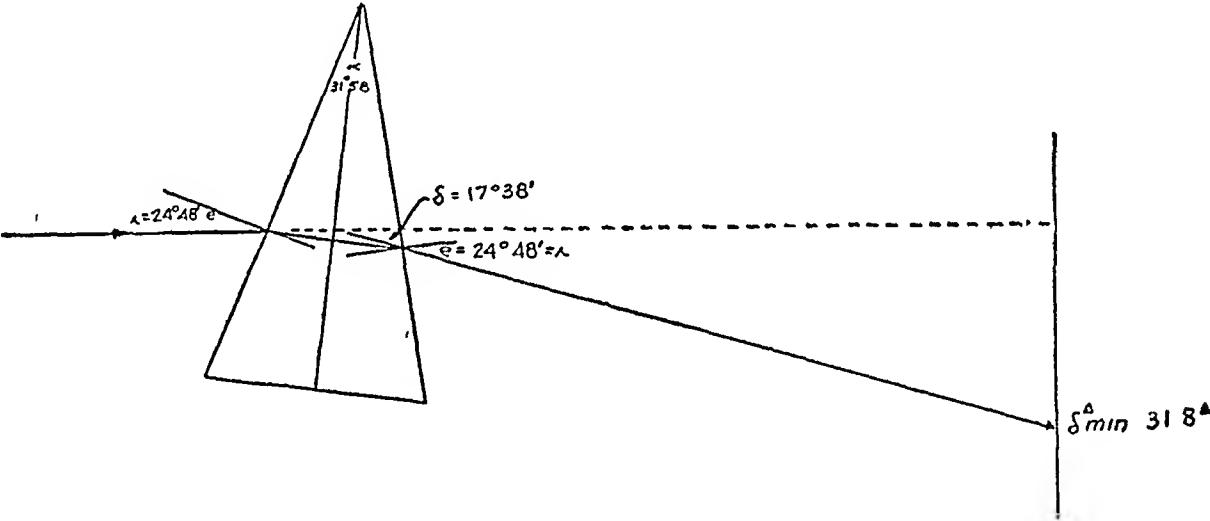


Fig 4—Deviation produced by a  $40 \Delta$  prism ( $31^{\circ} 58'$  apex angle) in the position of minimal deviation, in which  $i = e$

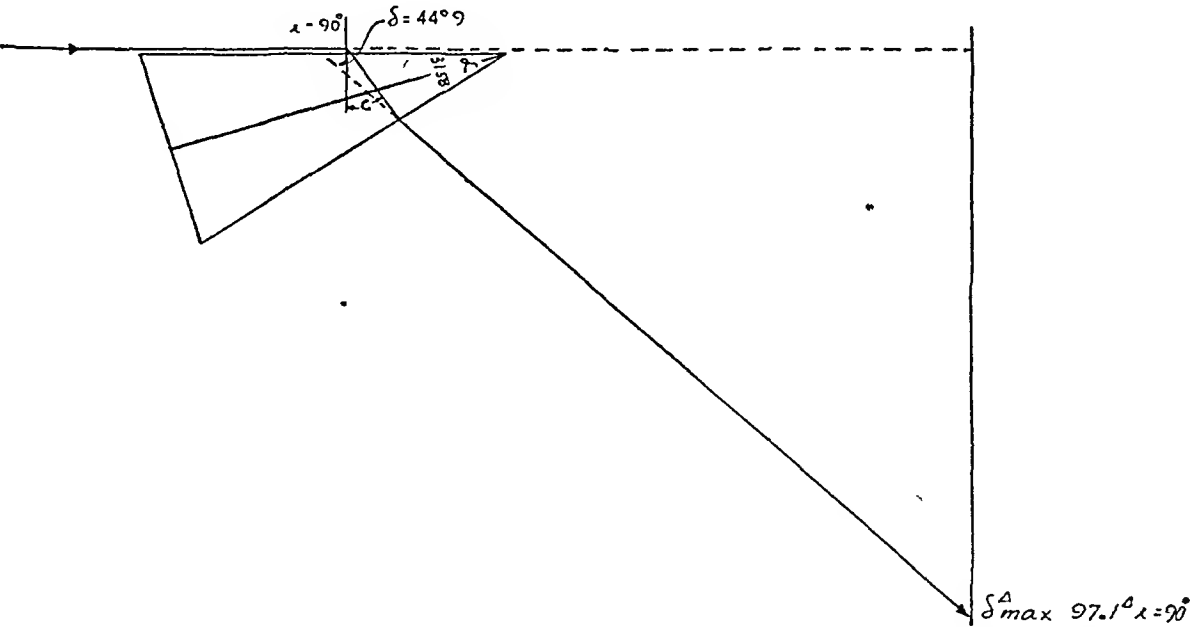


Fig 5—Deviation produced by a  $40 \Delta$  prism in the position of maximal deviation ( $i = 90^{\circ}$ )  
In this graph, and in that shown in figure 6, C indicates the critical angle ( $41^{\circ} 2'$ ) for glass with a refraction index ( $n'$ ) of 1.523

in the Prentice position, and the right hand boundary of the curve shows the maximal effect when  $e = 90^\circ$  (emergent ray grazes)

Note that whereas a 1  $\Delta$  prism has practically the same effect when held in the Prentice

A 20  $\Delta$  prism has an effect of 19  $\Delta$  in the position of minimal deviation and almost the same power in the split position, but it can be given a power of almost 75  $\Delta$  by improper positioning. If it is turned only  $30^\circ$ , so that

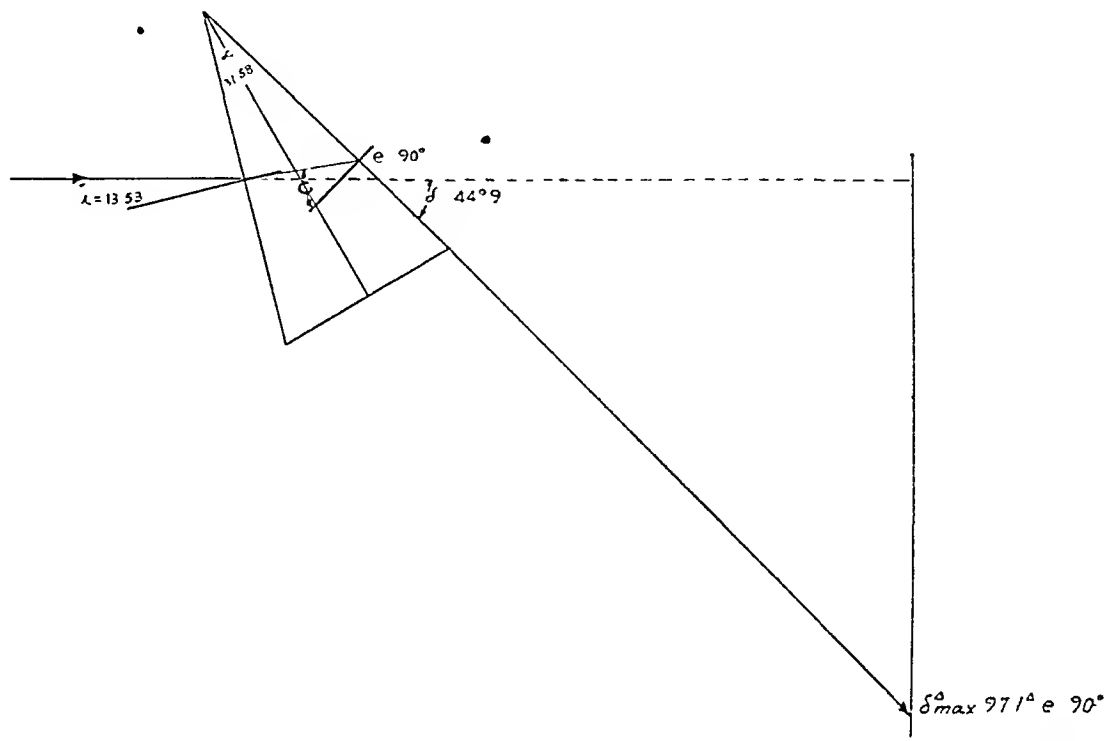


Fig 6—Deviation (97  $\Delta$ ) of a 40  $\Delta$  prism in the position of maximal deviation ( $e = 90^\circ$ )

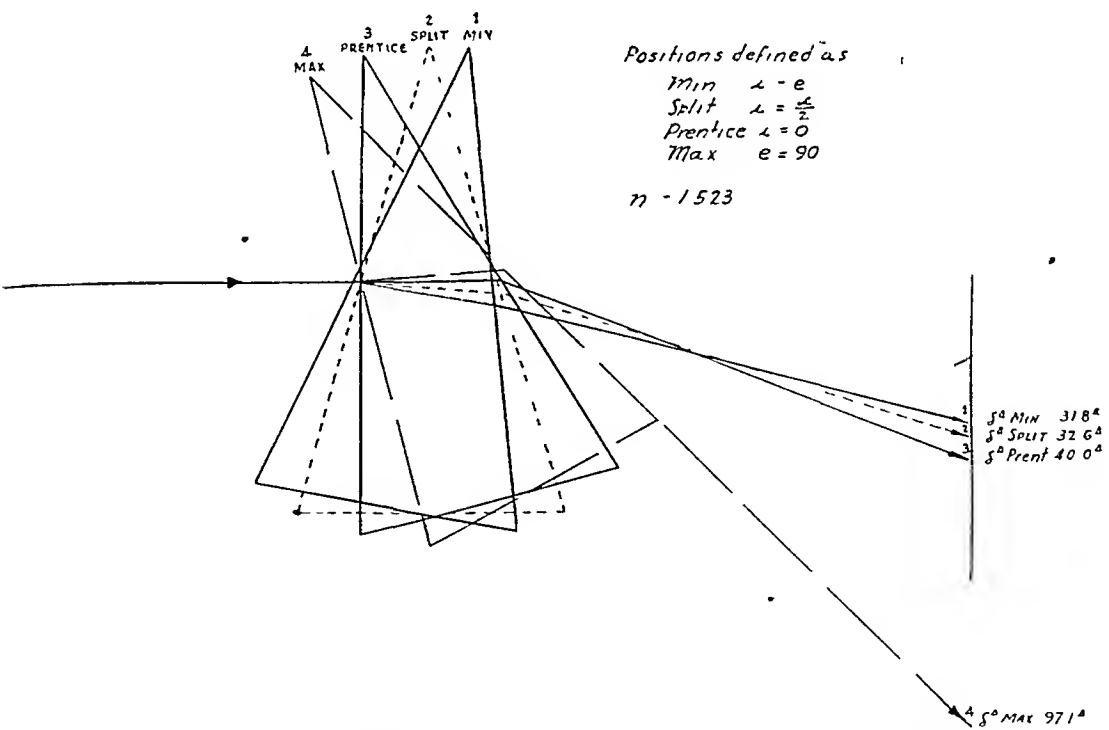


Fig 7—Composite illustration depicting the different deviations produced by the same 40  $\Delta$  prism as it is held in various positions relative to the entering ray

position, in the split position and in the position of minimal deviation, it can be made to produce an effect of 19.5  $\Delta$  if improperly positioned. Practically this is not a serious error, since there is little or no chance of such mishandling

the incident ray approaches from the apex side of the normal, it will exert a power of over 44  $\Delta$ . Metric prisms used for measuring squint usually come in sets of strengths up to 50  $\Delta$ . Note how dangerous the Prentice position is

at this value A 50  $\Delta$  prism has a minimal deviation of 36.46  $\Delta$ , a deviation of 37.65  $\Delta$  in the split position but may be given a maximal deviation of 103.61  $\Delta$  with improper holding, and it needs to be rotated less than  $9^\circ$  to produce

Even at 40  $\Delta$  a valuable lesson is to be drawn from figure 9. It has been seen in figures 2 to 8 how a 40  $\Delta$  prism behaves in effect. To rotate a 40  $\Delta$  prism  $10^\circ$  toward the apex increases its effect to 57  $\Delta$ , introducing an error

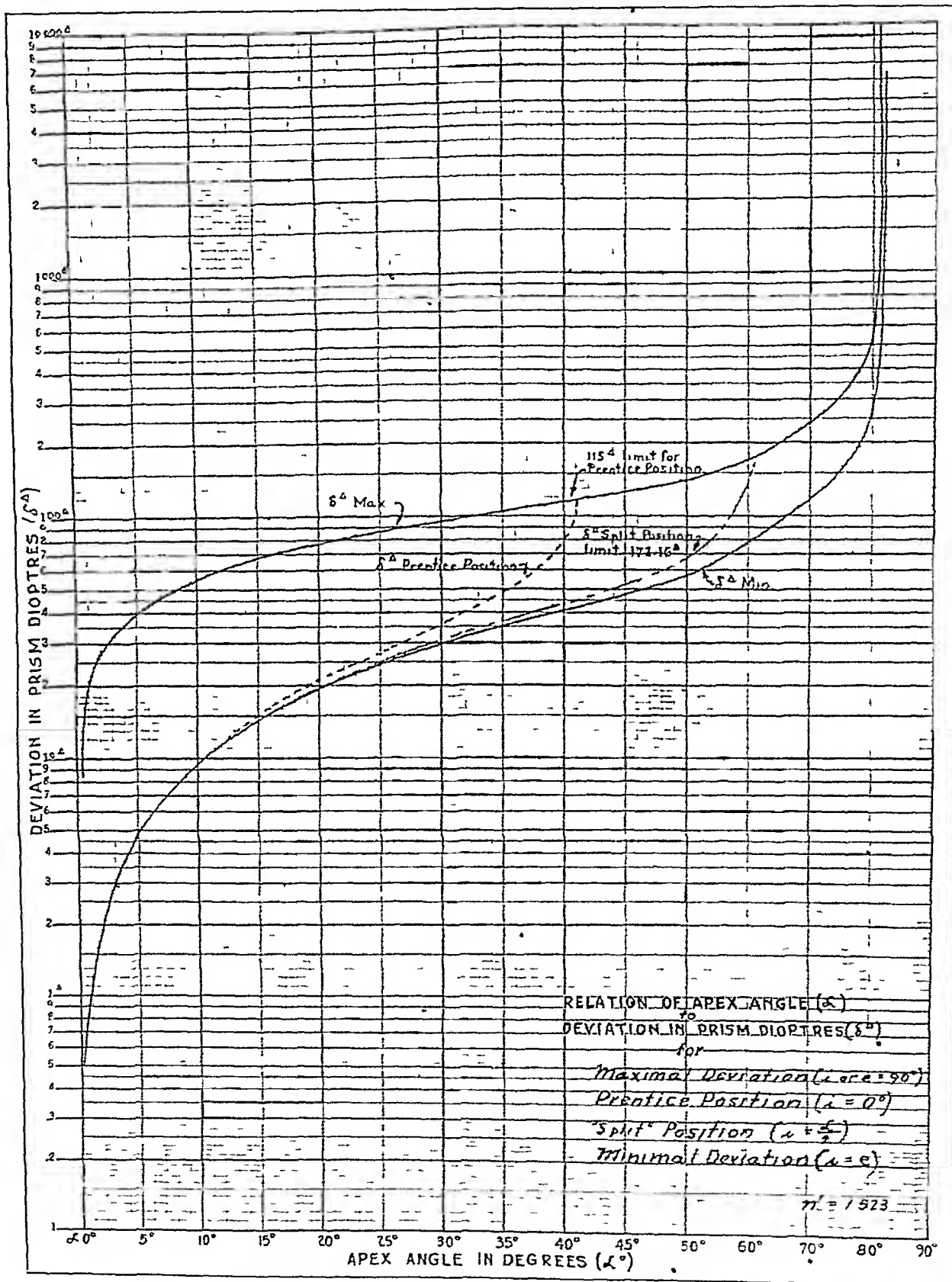


Fig 8—Relation of apex angle of prisms, to deviation in prism diopters

this effect. This is an important fact which is not widely known and seldom guarded against, and it partly explains why many ophthalmologists stop using prisms at about 40  $\Delta$  and rely on guesswork beyond that point.

of 17  $\Delta$ . If, however, two 20  $\Delta$  prisms were utilized, one over each eye, and the same error committed with each, the total effect would amount to only  $2 \times 27$  or 54  $\Delta$ . It is thus obvious that in measuring the higher degrees of

squint less error is introduced when the prism strength is divided between the two eyes

It is apparent that maximal errors will not often occur except when high power prisms are carelessly used. It is equally obvious from figure 9 that the position of minimal deviation is the safest position to use in safeguarding

ago, but since it is a variable position, it has found scant support

The split position is the one which is intuitively widely used, and it is good fortune that it deviates from the Prentice position toward the position of minimal deviation. While it is not the ideal, it represents an escape from the dan-

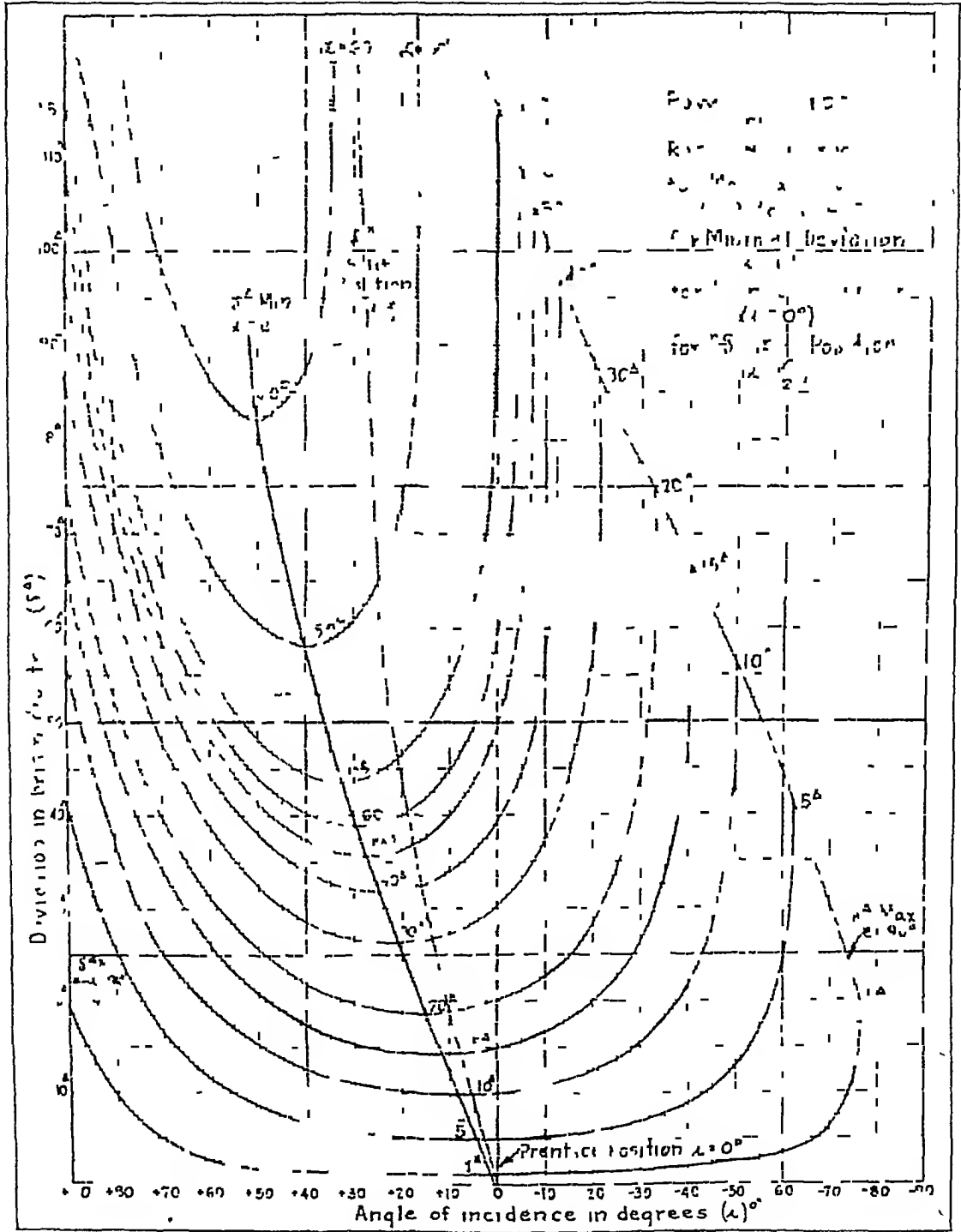


Fig 9—The power effect of rotating prisms

against error and that the Prentice position occupies a dangerous area of the curves. The position of minimal deviation was the one earnestly advocated by Jackson<sup>5</sup> many years

ago, but since it is a variable position, it has found scant support. The split position is the one which is intuitively widely used, and it is good fortune that it deviates from the Prentice position toward the position of minimal deviation. While it is not the ideal, it represents an escape from the dan-

5 Jackson, E. The Designation of Prisms by the Angular Deviation They Cause Instead of by the Re-

fracting Angle, Tr Internat M Cong (Sect 11, Ophth) 3:785, 1887

prisms in photometers and similar instruments, must mechanically be set

The changes in power of a prism due to the holding position have been discussed from only one point of view, i. e., the changes which result when the prism has been rotated about its major axis from the Prentice position. The major axis may be described as the axis joining the geometric centers of the plane parallel sides of the prism. It is a line bisecting the apex angle and lying parallel to the apex of the prism (Z axis, fig 10)

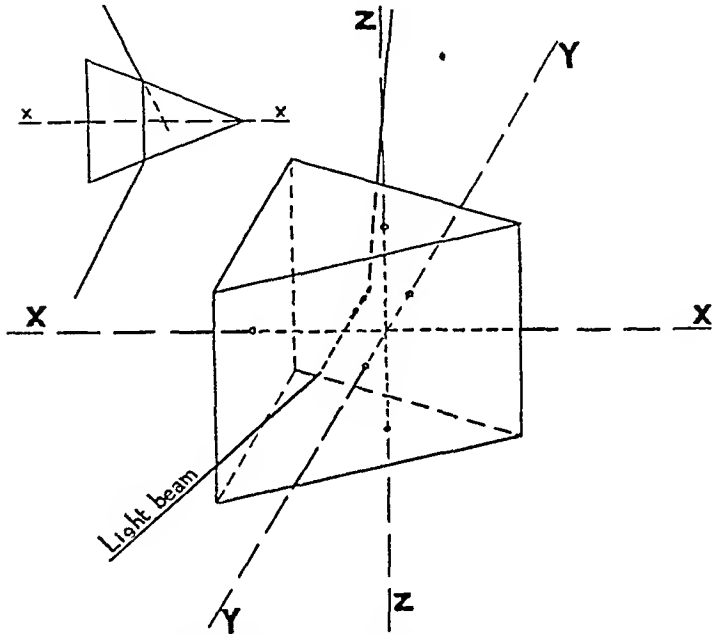


Fig 10—Major axes of a prism

There are two other axes of a prism. One, the face axis (or fore and aft axis), is a line joining the centers of the inclined faces of the prism. (This line would be parallel to the base in a symmetric prism [Y axis, fig 10]) It is the line describing the path of the internal light ray when the prism is held in the position of minimal deviation. Rotating the prism about this axis would convert a horizontal deviation into a vertical deviation, i. e., it would change

the position of the prism from base horizontal to base down or base up. With increasing rotation the amount of deviation produced by the prism in the horizontal meridian is reduced, while an increasing vertical component is added.

Rotating the prism about the third axis, which bisects the apex angle and is equidistant from the parallel surfaces (X axis, fig 10), results in spatial distortion and some change in power. The path of the ray inside the prism is prolonged. The geometric principles involved in this change have been described by Southall.

Finally, the distance from the eye at which the prism is held will change its effectivity. The farther from the eye the prism is held, the less is its effective deviational power. This is analogous to the change in effectivity produced by changing the distance from the eye in which the lens is held.

#### SUMMARY

The clinical use of ophthalmic prisms for measuring deviations of the eyes involves little known but serious dangers of committing error, particularly in the higher powers.

The units of prism strength are not usually marked on the prisms, and since several units are in use, this dereliction should be remedied.

Great care should be used in positioning metric prisms to avoid error.

If errors in positioning are made, it is much safer to err on the side of inclining the prism toward the position of minimum deviation than away from it.

The split position is a natural and intuitive manner of holding metric prisms which tends to avoid the dangers of the Prentice position.

In measuring high degrees of deviation, it is much safer to divide the prisms, holding approximately half the amount over each eye.

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# CATARACT AND OTHER CONGENITAL DEFECTS IN INFANTS FOLLOWING RUBELLA IN THE MOTHER

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Recent observations, particularly from Australia, seem to indicate that rubella during early pregnancy may lead to multiple serious congenital defects in the offspring. This was first noted in 1941 by Gregg<sup>1</sup> following a severe Australian epidemic of German measles. It is thought that crowding and troop movements may have made possible the rapid transfer of the virus from one person to another, and thus not only may have spread the epidemic but also may have caused some change in the virus.

Gregg described 78 cases of congenital cataract, 20 examined personally and the remainder reported to him by his colleagues. In 68 of these cases there was a definite history of German measles in the pregnant mother. Cardiac lesions were present in at least 44 of the 78 infants. A research team sponsored by the National Health and Medical Research Council of Australia, consisting of Drs Swan, Tostevin, Moore, Mayo and Black, carried out a widespread investigation by examination and questionnaire, reporting their results in two papers.<sup>2</sup> They found that of 61 mothers who contracted German measles during pregnancy, 41 bore children with congenital defects. These babies were abnormally light in weight even if born at term. There were 15 cases of cataract, 1 of buphthalmos, 3 of microphthalmos, 12 of deaf-mutism, 21 of cardiac abnormalities, at least 15 cases of some degree of microcephaly, and 1 case each of hypospadias, obliteration of the bile ducts and talipes equinovarus. Mental deficiency was probably present in several children. Swan and his associates are under the impression that the type of defect is somewhat determined by the stage of pregnancy at which rubella is contracted.

Thus the average duration of pregnancy in the mothers whose offspring had cataract was one and four-tenths months while the duration in those whose infants were deaf-mutes was two and three tenths months. The authors stated that "on the available evidence, when a woman contracts rubella within the first two months of pregnancy it would appear that the chances of her giving birth to a congenitally defective child are in the region of 100 per cent, and if she contracts rubella in the third month they are about 50 per cent." Evans, after studying some of the cases reported by Swan and his associates, stated that of 34 babies whose mothers suffered during pregnancy from rubella, 23 exhibited congenital dental abnormalities. These dental defects consisted of retardation of eruption, enamel hypoplasia and dental caries.

Reese,<sup>4</sup> in 1944, published the first American report on the association between German measles and congenital defects, with observations on 3 New York infants. All had cataracts and congenital heart defects. Rones,<sup>5</sup> from Washington, D C, reported the occurrence of cataract in 2 infants whose mothers had contracted rubella during the second month of pregnancy and 1 case of congenital glaucoma in an infant whose mother had become infected during the third month. Erickson<sup>6</sup> described 11 California infants with congenital cataract, 9 of whom also had defects of the heart.

These reports, from widely scattered sources, point out the necessity for further observations on what appears to be one of the important factors in the development of several congenital defects. We shall describe 6 cases that we have personally observed.

1 Gregg, N M. Congenital Cataract Following German Measles in Mother, *Tr Ophth Soc Australia* **3** 35-46, 1941.

2 (a) Swan, C, Tostevin, A L, Moore, B, Mayo, H, and Black, G H B. Congenital Defects in Infants Following Infectious Diseases During Pregnancy, *M J Australia* **2** 201-220 (Sept 11) 1943. (b) Swan, C, Tostevin, A L, Mayo, H, and Black, G H B. Further Observations on Congenital Defects in Infants Following Infectious Diseases During Pregnancy, with Special Reference to Rubella, *ibid* **1** 409-413 (May 6) 1944.

3 Evans, M W. Congenital Dental Defects in Infants Subsequent to Maternal Rubella During Pregnancy, *M J Australia* **2** 225-228 (Sept 2) 1944.

4 Reese, A B. Congenital Cataract and Other Anomalies Following German Measles in the Mother, *Am J Ophth* **27** 483-487 (May) 1944.

5 Rones, B. The Relationship of German Measles During Pregnancy to Congenital Ocular Defects, *M Ann District of Columbia* **13** 285-287 (Aug) 1944.

6 Erickson, C A. Rubella Early in Pregnancy Causing Congenital Malformations of Eyes and Heart, *J Pediat* **25** 281-283 (Oct) 1944.

## REPORT OF CASES

CASE 1 (J R N)—The mother contracted rubella when three or four weeks pregnant during a mild epidemic in St Louis. The disease apparently was acquired from a daughter, who in turn had been exposed to a case of German measles. The disease in the mother consisted of sore throat, cervical adenopathy and a marked eruption on the face with some lesions on the arms. She was not confined to bed and did not consult a physician. The mother stated that she had previously had rubella when 7 or 8 years of age. She had 1 healthy daughter, aged 3. There was no family history of congenital eye or heart defects.

The patient, a boy, was born on Dec 31, 1943, weighing 4 pounds, 4 ounces (1,927.76 Gm). Dr H. Rommel Hildreth saw the baby shortly after birth and made a diagnosis of congenital cataract of the right eye with slight microphthalmos. Our examination a year later confirmed these findings. The baby fixed on a light and showed an interest in the environment. The right eye was convergent to a variable amount, approximately 20 to 25 degrees. The right eyeball, including the cornea, was smaller than the left. The pupils were approximately equal in size and both reacted briskly to light. Both pupils dilated well with homatropine hydrobromide and paredrine hydrobromide. The right lens was diffusely hazy with a sharply demarcated dense central opacity. A dull fundus reflex, but no details, could be seen through the periphery of the lens. The anterior segment of the left eye, including the lens, seemed normal. The vitreous was hazy, and there were numerous moderately large opacities. The disk seemed abnormally pale. The entire posterior pole showed a diffuse mottled pigmentation as though from a mild chorioretinitis. The infant accurately fixed the ophthalmoscope light on the macula. Examination, including tonometry, under a general anesthetic was contemplated but not done owing to a severe congenital defect of the heart, thought to be a patent interventricular septum.

CASE 2 (K A)—The mother, aged 44, had German measles probably the first month or six weeks of pregnancy. A daughter acquired the disease during an epidemic at Kremmling, Colo., and communicated the infection to the mother and to another daughter. The mother had not previously had rubella. She was not very sick with the German measles but did have considerable cervical adenopathy, and about a week later varicose veins and pulmonary disturbance developed. The mother had previously had seven normal children. There was no family history of any congenital defect.

The patient, a boy, was born on March 9, 1943, weighing 5 pounds 15 ounces (6,803.88 Gm). There was a definite feeding problem, and he had several attacks of cyanosis. General examination revealed a congenital lesion of the heart, probably a septal defect. On April 12, 1943, the right cornea seemed slightly steamy and the pupil was dilated and fixed to light. The right fundus could be seen, showing some diffuse mild pigmentary disturbance. The left eye was distinctly smaller than the right, and the lens was cataractous. The entire lens was partially opaque, but the opacity in the pupillary zone was definitely more dense. The left pupil reacted normally to light. It was thought that the right eye was probably glaucomatous, so a salt of pilocarpine was prescribed. On July 16, 1943, the general condition having improved sufficiently to permit it, examination was carried out under general anesthesia. The intraocular pressure was 17 mm in

the right eye and 20 mm in the left eye (Gradle-Schiotz). The right cornea had lost its steamy appearance, and both pupils reacted briskly to light. The mild, diffuse disturbance of the chorioretinal pigment of the right eye was confirmed. The intraocular pressure has since been rechecked and found normal. The boy is alert and has developed well. He apparently has good vision in the right eye.

CASE 3 (G B B)—The mother had German measles when four to six weeks pregnant, while living in Cripple Creek, Colo. The rash first appeared on the abdomen, later spreading to the chest and face. Slight cervical lymphadenopathy was present. She was not confined to bed but a physician was called, who confirmed the diagnosis of rubella. This was the first pregnancy. There was no family history of any congenital defect.

The baby, a boy, was born at term, on Dec 31, 1942, weighing 6 pounds 10 ounces (3,005.05 Gm). Both eyeballs were abnormally small on gross inspection. Bilateral cataracts were observed shortly after birth. The entire pupillary area was opaque in both eyes. The pupils were small and did not dilate well with mydriatics. A discission was done on the right eye on Feb 16, 1943, but a clear pupil was not obtained. On Sept 28, 1943, a discission was done on the left eye, a vertical incision being made through a soft membranous cataract. A clear opening was immediately apparent. A second discission was done on the right eye on Sept 26, 1944. The baby has a congenital heart lesion, probably a septal defect, and bilateral cryptorchid testes. General development has been retarded, and the child has been slow in walking and talking.

CASE 4 (R L T)—The mother, aged 18 years, contracted German measles from a daughter when about three weeks pregnant, while living in Loveland, Colo. A sister also became infected at the same time. The mother had a generalized rash but was not confined to bed. The diagnosis of rubella was confirmed by a physician. The mother stated that she probably had rubella in childhood. There was one other child, aged 3 years, in good health. There was no family history of any congenital defect.

The baby, a boy, was born at term on Dec 11, 1942, weighing 4½ pounds (2,041.16 Gm). He did not void until catheterized but has had no further urinary difficulty. There was a slight valgus deformity of the right foot. The heart was definitely abnormal, the heart sounds being largely obliterated by a loud murmur. He presented a feeding problem. On Jan 25, 1945 an examination was made under general anesthetic and a discission of a cataract of the right eye was done. The right eye was definitely smaller than the left. The right cornea measured 9.7 mm in the horizontal meridian while the left measured 11 mm. The entire right lens was hazy, but the central zone showed a dense, sharply delimited opacity. The left eye seemed normal except for a diffuse pigmented mottling of the fundus with the greatest irregularity of pigmentation in and temporal to the macular region. Since the discission the lens material has shown little tendency to absorb.

CASE 5 (G C K)—The mother, aged 31, had German measles when about four weeks pregnant, while living in Denver. The illness began with a slight sore throat and malaise followed by an eruption of the arms, face and torso. The eruption lasted for three days, during which time the mother remained in bed but was not especially ill. There was no family history of any congenital defect.



The baby, a girl, was born on Dec 8, 1944, weighing 6 pounds 5 ounces (2,863.3 Gm). She was cyanotic at times and was difficult to feed. Roentgenograms of the chest showed a transverse enlargement of the heart. Clinical signs were suggestive of an interventricular septal defect. When examined on Feb 12, 1945, the baby seemed to be in fair general condition. Both eyes showed a mucopurulent secretion, and this material could be expressed from both tear sacs. Both eyes were abnormally small, especially the right. The pupils reacted sluggishly to light and dilated poorly with homatropine and paredrine hydrobromide. Both lenses were densely opaque with a suggestion that the periphery might be clearer. Inadequate mydriasis made it impossible to examine more than the central area.

Not directly connected with this case, but worthy of note, is the observation that the mother presumably transmitted the disease to Mrs. N. W., a neighbor, who was then three and one-half months pregnant. Mrs. N. W.'s baby was stillborn as the result of an obstetric accident. The eyes were not examined. Autopsy disclosed a normal heart.

**CASE 6 (J. W. T.)**—The mother, aged 30, had a rash, presumably German measles, two weeks after her last menstrual period. This rash involved her face, with a few scattered lesions over the body. She did not feel well but did not go to bed. She does not remember many details of the illness and considered it trivial at the time. A daughter and several children living in the same block in Denver had German measles at the same time. The mother has one child in good health and has had one stillborn child. The mother's father and one brother have mild hypospadias. There was no other family history of congenital defects.

The baby, a boy, was born at term on Nov 1, 1943, weighing 5 pounds 2 ounces (2,324.66 Gm). The infant has presented a persistent feeding problem. At the age of 15 months he weighed 13 pounds 9 ounces (6,151.84 Gm). There was a congenital heart defect producing a murmur heard throughout the cycle. The lesion was thought to be a patent ductus arteriosus. The infant was tongue-tied, and hypospadias of the penile portion was present. We first examined the boy on Feb 11, 1945. He was seemingly alert and made an effort to look at objects. There was an inconstant and variable convergent strabismus. The eyes made coarse nystagmoid movements. Both eyeballs, including the corneas, were definitely smaller than normal. The pupils were equal and reacted moderately to light. Both lenses were quite opaque in the pupillary zones and no fundus reflex could be obtained. A mydriatic was not used.

#### COMMENT

In all 6 of the cases described rubella had developed in the mothers during the first two to six weeks of pregnancy. Three of the mothers did not know that they were pregnant when the exanthem appeared. The disease was mild and usually regarded as trivial. Few of the mothers remembered many of the details of the illness. In all of the cases there was a history of contact with some one suffering from rubella and in several cases there were multiple infections in the family. Five of the infections were acquired in Colorado and one in St. Louis. The earliest case was in 1942.

All of the babies had congenital cataracts. In 3 cases the cataracts were bilateral and the lenses more or less completely opaque. One of the cataracts (case 3) apparently was membranous. There were 3 bilateral and 3 unilateral cases of microphthalmos. The corneas were measured in only 1 baby, but the defect was grossly apparent in all. The unilateral cataracts were primarily nuclear with a less opaque periphery. These nuclear cataracts conformed closely with the description given by Gregg.<sup>1</sup> Each of these 3 patients showed in the non-cataractous eye diffuse pigment alteration in the fundus suggestive of changes resulting from chorioretinitis. Swan and associates<sup>2</sup> described "multiple small pigmented spots on the fundus" in 1 case. Vitreous opacities were found associated with the changes in the fundus in case 1. Sluggish pupillary reactions have been noted by most observers. In 2 of our cases it was our impression that the pupils reacted sluggishly shortly after birth but that the reaction was normal when the eyes were examined approximately one year later. In 2 of the infants the pupils failed to dilate well with several different mydriatics. One of the patients (case 2) had a hazy cornea that later cleared. Bilateral congenital dacryostenosis was present in case 5. It would seem that all of the intraocular findings can be explained on the basis of an intrauterine inflammatory reaction involving particularly the uveal tract.

Some type of cardiac lesion was present in all 6 of the babies, a septal defect being suspected in 4. The infants were somewhat smaller than average. Most had some difficulty in feeding. Microcephalus was not observed, but no measurements of the head were made. There was no attempt to evaluate the mental condition. There was 1 case each of talipes valgus and of cryptorchism. The patient with hypospadias had a strong family history of this condition, so we probably cannot ascribe this defect to the maternal rubella.

As rubella is a common disease, and as it doubtless in the past has infected a great many pregnant women, one may ask why this relationship to defects in the offspring had not been noted prior to 1941. This omission is particularly striking when one considers that common defects include a distinctive type of cataract and microphthalmos. It would seem probable that some new factor has developed to produce the congenital defects. Gregg<sup>1</sup> has expressed some doubt as to the disease being rubella. Swan and associates<sup>2</sup> studied this question carefully and concluded that the infection is rubella but that

the disease may have undergone some alteration in character. They<sup>2b</sup> later pointed out other evidence indicating some change in the disease. One may conjecture that the virus of rubella underwent some transformation in Australia and that this new strain was introduced into the United States. The introduction would not have been difficult with the current voluminous and rapid traffic between these countries.

In view of the serious malformations encountered every effort should be made to protect women in early pregnancy from rubella. Erickson<sup>6</sup> recommended the deliberate exposure of girls to rubella to immunize them before the child-bearing age. He further suggested the use, particularly during epidemics, of convalescent serum for all women who are in early pregnancy and have not had rubella. Strong<sup>7</sup> suggested that gamma globulin may prove of value in modifying the immunity to the disease.

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7 Strong, R. A. Rubella and Congenital Malformations, editorial, *Internat M Digest* 46 60-62 (Jan) 1945

Therapeutic abortion has been recommended if rubella should occur during the first third of pregnancy. The gravity of the congenital lesions and the likelihood of their development would possibly seem to warrant this procedure.

#### CONCLUSIONS

Congenital defects have been observed in six infants whose mothers had contracted rubella when from two to six weeks pregnant. Three of the babies had bilateral cataracts which were associated with bilateral microphthalmos. Three of them had unilateral microphthalmos with a distinctive type of cataract in the smaller eye. Lesions were observed in the fundus in the three eyes of this series in which the fundus could be seen. All 6 children had cardiac defects. There was 1 case each of talipes valgus, cryptorchism, hypospadias and dacryostenosis. We believe that the cataracts, the microphthalmos, the lesions of the fundus and the cardiac defects are the result of intrauterine damage by rubella.

# EVALUATION OF TOXOPLASMA NEUTRALIZATION TESTS IN CASES OF CHORIORETINITIS

JOSEPH M HEIDELMAN, M D

CINCINNATI

The purpose of this paper is to report the results of a study of the possible diagnostic significance of Toxoplasma-neutralizing antibodies in determining the cause of chorioretinitis

## REVIEW OF LITERATURE

*Epidemiology*—Toxoplasma is a protozoon of uncertain classification first observed in the North African rodent gondi and named by Nicolle and Manceau<sup>1</sup> in 1909. Since then a large number of animal species, including birds, from various parts of the world have been described as natural hosts for this parasite. Animal toxoplasmosis is



Fig 1—Toxoplasmas in a smear from the brain of a mouse. Wright's stain,  $\times 950$

considered the source of human infection, although the manner of transmission among animals and from animals to man is unknown. The biologic and immunologic relationship between a human and an animal strain of Toxoplasma has been demonstrated<sup>2</sup>

*Properties of Toxoplasma*—In strained smears (fig 1) the organisms are crescentic, oval or

From the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital and University.

1 Nicolle, C., and Manceau, L. Sur un protozoaire nouveau 'du gondi' Toxoplasma n. gen., Arch Inst Pasteur de Tunis 2: 97-103, 1909.

2 Wolt, A., Cowen, D., and Paige, B. H. Human Toxoplasmosis: Occurrence in Infants as an Encephalomyelitis. Verification by Transmission to Animals, Science 89: 226-227 (March 10) 1939. Sabin, A. B. Biological and Immunological Identity of Toxoplasma of Animal and Human Origin. Proc Soc Exper Biol & Med 41: 75-80 (May) 1939.

piriform in shape measuring 4 to 7 microns in length and 2 to 4 microns in width. They consist of a distinct cytoplasm and a nuclear chromatin mass. With Wright's stain the nuclear chromatin is deep purple and the cytoplasm pale blue. In fixed tissues toxoplasmas are smaller and more rounded and often bear little resemblance to those observed in smears. They often occur in clusters or aggregates, commonly referred to as cysts



Fig 2—Toxoplasmic chorioretinitis, with parasitic "cyst" in the retinal lesion. Phloxine-hematoxylin stain,  $\times 1,050$  (from Koch, Wolf, Cowen and Paige<sup>3</sup>)

or pseudocysts (fig 2). The parasites are non-motile, and multiplication, which requires living tissues,<sup>3</sup> is by binary fission in the longitudinal plane.

*Toxoplasmosis in Man*—The occurrence of human toxoplasmosis was first proved in 1939, when Wolf, Cowen and Paige<sup>4</sup> demonstrated

3 Sabin, A. B., and Olitsky, P. K. Toxoplasma and Obligata Intracellular Parasitism, Science 85: 336-338 (April 2) 1937.

4 Wolf, A., Cowen, D., and Paige, B. H. Toxoplasmic Encephalomyelitis. III. A New Case of Granulomatous Encephalomyelitis Due to a Protozoan, Am J Path 15: 657-694 (Nov) 1939.

toxoplasmas at autopsy in the tissues of the central nervous system and the eye of an infant with encephalomyelitis and transmitted the infection to animals. There are at present 13 fatal cases of infantile toxoplasmosis on record. Nine of these cases, 4 of which were obtained from the literature<sup>5</sup> and had not previously been recorded as instances of the disease, were identified by Wolf and his associates<sup>6</sup>. One of the cases of the same authors had previously been reported by them as an instance of encephalitozoic encephalomyelitis<sup>6a</sup>. Of the remaining 4 cases, 2 were identified by Steiner and Kaump<sup>7</sup> and 2 by Zuelzer<sup>8</sup>. The diagnosis in 1 of the cases mentioned in the report of Steiner and Kaump was made by a restudy of the sections of the brain from a case referred to them by Salei. The case reported by Hertig,<sup>9</sup> of an infant who died presumably of bacterial infection and in whose tissues protozoa were found which were classified as *Sarcocystis* by the author but later were recognized as toxoplasmas by Pinkerton and Weinman,<sup>10</sup> is not included as an example of the same disease.

5 Janků, J. Pathogenesis and Pathologic Anatomy of Coloboma of the Macula Lutea in an Eye of Normal Dimensions, and in a Microphthalmic Eye, with Parasites in the Retina, *Časopis lékařů českých* **62** 1021-1027, 1054-1059, 1081-1085, 1111-1115 and 1138-1143, 1923. Margarinos Torres, C. Sur une nouvelle maladie de l'homme, caractérisée par la présence d'un parasite intracellulaire, très proche du *Toxoplasma* et de l'Encephalitozoon, dans le tissu musculaire cardiaque, le muscle du squelette, le tissu cellulaire sous-cutané et le tissu nerveux, *Compt. rend. Soc. de biol.* **97** 1778-1781, 1927. Richter, R. Meningoencephalomyelitis Neonatorum. Anatomic Report of a Case, *Arch. Neurol. & Psychiat.* **36** 1085-1100 (Nov.) 1936. de Lange, C. Klinische und pathologisch-anatomische Mitteilungen über Hydrocephalus chronicus congenitus und acquisitus, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **120** 433-500, 1929.

6 (a) Wolf, A., and Cowen, D. Granulomatous Encephalomyelitis Due to an Encephalitozoon (Encephalitozoic Encephalomyelitis), *Bull. Neurol. Inst. New York* **6** 306-371 (July) 1937. (b) Paige, B. H., Cowen, D., and Wolf, A. Toxoplasmic Encephalomyelitis. V. Further Observations of Infantile Toxoplasmosis, Intra-Uterine Inception of the Disease, Visceral Manifestations, *Am. J. Dis. Child.* **63** 474-514 (March) 1942. (c) Wolf, A., and Cowen, D. Toxoplasmic Encephalomyelitis, in Blumer, G. *Practitioners Library of Medicine and Surgery*, New York, D. Appleton-Century Company, Inc., 1940. (d) Wolf, Cowen and Paige.<sup>4</sup>

7 Steiner, G., and Kaump, D. H. Infantile Toxoplasmic Encephalitis. Report of a Case, *J. Neuropath. & Exper. Neurol.* **3** 36-48 (Jan.) 1944.

8 Zuelzer, W. W. Infantile Toxoplasmosis, with a Report of Three New Cases, Including Two in Which the Patients Were Identical Twins, *Arch. Path.* **38** 1-19 (July) 1944.

9 Hertig, A. T. Sarcosporidia in the Myocardium of a Premature Infant. Report of a Case, *Am. J. Path.* **10** 413-418 (May) 1934.

*Clinical Picture*—Fatal cases of toxoplasmic encephalomyelitis, as noted by Wolf and his co-workers, were characterized chiefly by convulsions, internal hydrocephalus, cerebral calcification and other neurologic symptoms or signs, and chorioretinitis. The spinal fluid was commonly xanthochromic, with increased protein and mononuclear pleocytosis.

*Pathologic Features*—The pathologic changes in the central nervous system, according to the same authors,<sup>11</sup> consisted of areas of inflammation and necrosis and miliary granulomas, hydrocephalus and calcification. In some cases lesions were found in other organs, and in 1 case there was predominantly visceral involvement.<sup>6b</sup>

Similar areas of inflammation and necrosis were found in the retina (fig. 3). In the central portions of the necrotic areas all the layers of the retina were involved with perivascular and diffuse infiltration of lymphocytes, plasma cells and occasional neutrophils, eosinophils and lipid-laden phagocytes. There was endothelial hyperplasia of the capillaries, and an increase in glial tissue was sometimes seen, with extension into the vitreous. Disruption of the lamina including the pigment layer occurred in the more affected zones, with migration of pigment into the inner retinal layers. In areas corresponding to the retinal lesions the choroid was infiltrated with cells similar to those in the retina, and the sheaths of the optic nerve were similarly infiltrated. The sclera was normal. Toxoplasmas were present in the chorioretinal lesions (fig. 2).

*Prenatal Inception of Disease*—In 1 of the cases of Wolf, Cowen and Paige<sup>12</sup> intrauterine hydrocephalus required craniotomy for delivery, in other cases the presence of symptoms during the first days of life or the pathologic age of the lesions suggested onset of infection before birth. Since all the mothers appeared healthy, the implication was that they harbored a latent infection. The possibility of the existence of an acquired type of infantile toxoplasmosis was mentioned by Sabin<sup>13</sup> and by Cowen, Wolf and Paige<sup>14</sup> and was recently considered by Zuelzer<sup>8</sup> in 1 of his cases.

10 Pinkerton, H., and Weinman, D. *Toxoplasma Infection in Men*, *Arch. Path.* **30** 374-392 (July) 1940.

11 Wolf, Cowen and Paige.<sup>4</sup> Wolf and Cowen.<sup>6a</sup> Paige, Cowen and Wolf.<sup>6b</sup>

12 Wolf, A., Cowen, D., and Paige, B. H. Fetal Encephalomyelitis. Prenatal Inception of Infantile Toxoplasmosis, *Science* **93** 548-549 (June 6) 1941.

13 Sabin, A. B. Toxoplasmosis, in De Sanctis, A. G. *Advances in Pediatrics*, New York, Interscience Publishers, Inc., 1942.

(Footnotes continued on next page)

*Other Forms of Toxoplasmosis*—Acquired toxoplasmosis was encountered in 2 children in the form of an atypical encephalitis by Sabin,<sup>15</sup> with survival in 1 case, and in 3 adults as an acute fatal exanthematous disease with pulmonary involvement, 1 case being reported by Pinkerton and Weinman<sup>10</sup> and the other 2 by Pinkerton and Henderson<sup>16</sup>. In all cases toxoplasmas were identified in the tissues, the spinal fluid or the blood. Among the apparent clinical and pathologic differences between the congenital and the acquired disease, of interest here, is the complete absence of ocular involvement in the latter.

*Serologic Findings*—In 1937 Sabin and Olitsky<sup>3</sup> reported that *Toxoplasma*-neutralizing antibodies appeared in the serum of experimentally infected rhesus monkeys. The presence of this

mothers in these instances were themselves infected.

*Recognition of Congenital Toxoplasmosis During Life*—In 1941 Wolf, Cowen and Paige<sup>12</sup> mentioned the cases of 2 children in which the clinical diagnosis of toxoplasmic encephalomyelitis was made. These, with 4 other cases of infants or children who had a similar clinical picture, were described in a later report<sup>14</sup>. In most cases there was a history of onset of symptoms or signs early in life. Chorioretinitis, cerebral calcification and mental deficiency or psychomotor retardation were commonly associated features. Toxoplasmas were isolated by inoculation of mice with the ventricular fluid of a patient 2 months of age who had chorioretinitis, hydrocephalus and cerebral calcifica-

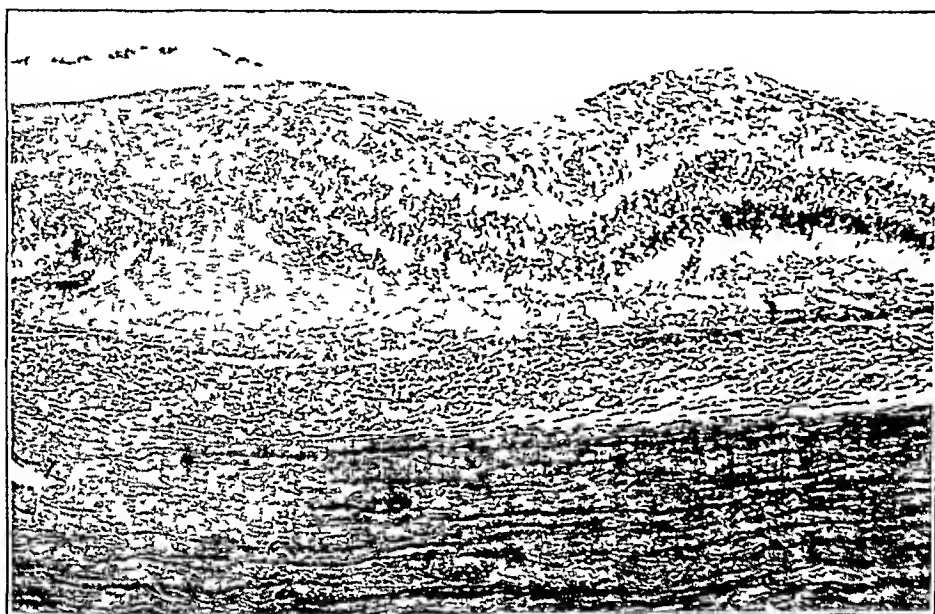


Fig 3—Toxoplasmic chorioretinitis, showing focal area of necrosis and inflammation in the retina and dense infiltration of the choroid. Phloxine-hematoxylin stain,  $\times 125$  (from Koch, Wolf, Cowen and Paige<sup>18</sup>).

antibody in human serum was reported for the first time by Sabin<sup>15</sup> in a fatal case of toxoplasmic encephalitis verified at autopsy. Using the serologic method of these investigators, Wolf, Cowen and Paige<sup>12</sup> demonstrated *Toxoplasma* antibodies in the serum of mothers of infected infants and thereby furnished additional support for the early suspicion that the

There was psychomotor retardation at the age of  $7\frac{1}{2}$  months. Forms resembling *Toxoplasma* were observed in a direct smear of ventricular fluid from another patient at  $3\frac{1}{2}$  months of age with the symptoms and signs just mentioned, and with epileptic seizures, which commenced in the fifth month of life. The serums of all 6 patients, whose ages ranged from 8 months to 11 years at the time the tests were made, had *Toxoplasma*-neutralizing antibodies, but this was true of only 2 of the mothers. The authors pointed out that the infection in the later phase may become inactive or healed, with the clinical manifestations occurring mainly as residual effects from the earlier period and that the abnormalities of infants surviving an attack of toxoplasmic encephalomyelitis may erroneously be classified as congenital malformation of the

14 Cowen, D., Wolf, A., and Paige, B. H. Toxoplasmic Encephalomyelitis. VI. Clinical Diagnosis of Infantile or Congenital Toxoplasmosis, Survival Beyond Infancy, *Arch Neurol & Psychiat* **48**: 689-739 (Nov.) 1942.

15 Sabin, A. B. Toxoplasmic Encephalitis in Children, *J A M A* **116**: 801-807 (March 1) 1941.

16 Pinkerton, H., and Henderson, R. G. Adult Toxoplasmosis. A Previously Unrecognized Disease Entity Simulating the Typhus-Spotted Fever Group, *J A M A* **116**: 807-814 (March 1) 1941.

brain, congenital hydrocephalus, birth injury, epilepsy, etc

In a publication which followed the preliminary report of Wolf and his associates, Sabin<sup>13</sup> described the case of an infant with chorioretinitis, cerebral calcification and hydrocephalus at 6 months of age. Ventricular fluid and biopsy specimens of the cortex were negative for *Toxoplasma*, but miliary granulomas were found in the tissue specimen. Psychomotor retardation was present at the age of 15 months. The diagnosis was corroborated by the same serologic method in the case of this patient and in the case of 8 other infants or children who had chorioretinitis or cerebral calcification or both associated with hydrocephalus or microcephaly or with convulsions and psychomotor retardation. The maternal serum was positive for *Toxoplasma* antibodies in every case.

Crothers<sup>17</sup> mentioned 10 cases in which the diagnosis of toxoplasmosis was supported by positive serologic reactions. There were 3 siblings in the group, 2 of whom had chorioretinitis, convulsions and cerebral calcification and the third the last condition only. Neutralizing antibodies were also found in the serum of normal members of the families of patients with clinical evidence of the disease, in addition to the mothers, whose serum regularly neutralized *Toxoplasma*.

*Ocular Picture*—In the series of 15 cases of toxoplasmic encephalomyelitis reported by Wolf and his associates, including those identified from the literature, in which the diagnosis was made either clinically or at autopsy, chorioretinitis was present in 10 of the 11 cases in which ophthalmoscopic examination was made. In a stillborn infant the chorioretinal lesions were found at autopsy. Three patients had no clinical or histologic examination of the eyes. The chorioretinitis as described ophthalmoscopically<sup>18</sup> was invariably bilateral, and, with the exception of one eye, there was always macular involvement. Two patients, 31 days and 4 years of age, respectively, had lesions which showed slight activity, otherwise the chorioretinitis was healed. The acute or subacute lesions were characterized by edema, early necrosis and pigmentation. The healed lesions were sharply circumscribed, atrophic areas, varying in size, number, degree of proliferation and pigmentation. Squint, microph-

thalmos, nystagmus and optic nerve atrophy were commonly associated. Remnants of pupillary membrane, posterior cortical cataract and lenticonus were occasionally present.

The lesions in Sabin's cases were macular in position, although the number in which chorioretinitis existed was not stated and further descriptions were not given.

The chorioretinitis which was present in 7 of 10 cases reported by Crothers was not described.

*Toxoplasma Antibodies Associated with Chorioretinitis or with Other Conditions*—Of 10 patients with chorioretinitis who were studied serologically by Sabin,<sup>19</sup> 9 had neutralizing antibodies. Four of these patients were children, 8 to 14 years of age, with visual disturbances noted earlier in life. Their mothers also had neutralizing antibodies. The other 6 patients, 5 of whom had antibodies, were adults 15 to 57 years of age at the time of onset of ocular symptoms. The lesions in 6 of Sabin's cases were described in a separate communication by Vail, Strong and Stephenson.<sup>20</sup> In general the lesions were similar to those in the cases of toxoplasmic chorioretinitis previously described. These authors suggested that a positive serologic reaction could be considered final evidence of a toxoplasmic origin in acquired as well as in congenital chorioretinitis.

Sabin<sup>19</sup> also found *Toxoplasma* antibodies in the serums of patients with unexplained encephalopathies or atypical pneumonia, of mothers who gave birth to anencephalic infants or infants with microcephaly or hydrocephalus and of normal persons,<sup>21</sup> including members of families of patients with clinical manifestations of toxoplasmosis.

#### MATERIAL FOR PRESENT STUDY

*Serums*—Neutralization tests were performed on the serums of 211 persons one or more times for a total of 269 tests. These serums were obtained from patients with various forms of uveitis or other types of congenital or acquired ocular disease and from normal persons, including parents of patients with congenital chorioretinitis.

The serums were taken from patients in the wards and clinics of the Wilmer Ophthalmological Institute and the Harriet Lane Home for Children's Diseases of the Johns Hopkins Hospital, from patients at the Baltimore City Hospitals and from students at the

19 Sabin, A. B. *Toxoplasma* Neutralizing Antibody in Human Beings and Morbid Conditions Associated with It, *Proc Soc Exper Biol & Med* **51**:6-10 (Oct) 1942.

20 Vail, D., Strong, J. C., Jr., and Stephenson, W. V. Chorioretinitis Associated with Positive Serologic Tests for *Toxoplasma* in Older Children and Adults, *Am J Ophth* **26** 133-140 (Feb) 1943.

21 These persons were laboratory workers or rabbit handlers.

17 Crothers, B. Toxoplasmic Encephalitis. Clinical Experience, *Arch Neurol & Psychiat* **49** 315-319 (Feb) 1943.

18 Koch, F. L. P., Wolf, A., Cowen, D., and Paige, B. H. Toxoplasmic Encephalomyelitis. VII. Significance of Ocular Lesions in the Diagnosis of Infantile or Congenital Toxoplasmosis, *Arch Ophth* **29** 1-25 (Jan) 1943.



Maryland School for Blind Children The normal serums were obtained from surgical, obstetric and newborn patients and from hospital employees

*Organisms*—Two strains of *Toxoplasma* were used in these tests One originated from a fatal case of encephalitis and the other from a case of encephalomyelitis with a similar termination<sup>22</sup>

#### TECHNIC

The method used for the determination of the presence or absence of neutralizing antibodies in serum was that described by Sabin and Olitsky<sup>3</sup> and by Sabin<sup>19</sup>

TABLE 1—Criteria Used in Interpretation of *Toxoplasma* Neutralization Test

Category of Unknown Serum	Relative Size of Cutaneous Lesions Yielded by Mixtures Containing Various Dilutions of Infected Mouse Brain Suspension			
	1 20	1 100	1 1,000	1 10,000
Negative	++++	++++	+++	++ or +
Negative	++++	++++	+++	—
Equivocal (repeat)	++++	+++	++ or +	—
Positive	++++ or +++	+++ or ++	—	—
Strong positive	++	—	—	—

TABLE 2—Incidence of Positive, Equivocal and Negative Results of Neutralization Tests on Various Types of Serum

	Serums Tested	Number			Per Cent		
		Positive	Equivocal	Negative	Positive	Equivocal	Negative
Congenital ehorioretinitis	27	11	6	9	41	22	37
Acquired ehorioretinitis	59	5	3	51	8.5	5	86.5
Acquired anterior uveitis	38	1	3	34	2.5	8	89
Normal subjects							
(a) Mothers of patients with congenital ehorioretinitis	7	5	1	1	70	14.5	14.5
(b) Fathers of patients with congenital ehorioretinitis	2	0	1	1	0	50	50
(c) Others	58	4	2	52	7	3	90

*Procedure*—Sterile precautions are observed in the collection of blood and the performance of the test Because of the marked heat lability of the antibody, the serum is either tested on the day the blood is obtained or is frozen rapidly in sealed tubes and stored in a carbon dioxide refrigerator or preserved by means of lyophilization until used<sup>23</sup>

*Toxoplasmas* are maintained for use by regular intracerebral passage of infected mouse brain suspension in the same species, death usually occurring between the fourth and the sixth day after inoculation

At least two mouse brains are used in the test These are removed when the animals are moribund and are weighed and ground in a mortar without an abrasive A 10 per cent tissue suspension is made by the addition of Tyrode's solution<sup>24</sup> This is allowed to precipitate spontaneously for thirty minutes in a refrigerator, after which the cloudy supernatant liquid is removed from the coarser particles From the former, designated as the 1 10 dilution, dilutions of 1 50,

22 These strains were furnished by Dr A Sabin and by Dr A Wolf respectively

23 Negative tests which were obtained with serum kept at room temperature seventy-two hours or longer are not included in this series

24 Isotonic solution of sodium chloride was substituted for Tyrode's solution in 198 tests because of the ready contamination of the latter

1 500 and 1 5,000 are prepared with Tyrode's solution as the diluent Equal amounts (0.15 cc) of each serum to be tested (Tyrode's solution is used as the control) and 0.15 cc of each dilution of the suspension of toxoplasmas are mixed in small tubes, resulting in final dilutions of 1 20, 1 100, 1 1,000 and 1 10,000 of all mixtures After thirty minutes at room temperature, 0.2 cc of each mixture is injected intradermally on the back of a shaved, clear-skinned rabbit into areas marked off with an indelible pencil

During the early period of observation an injection wheal and the erythema reaction to serum appear but shortly subside *Toxoplasma* lesions make their appearance after several days and increase in size until the seventh or eighth day They are elevated indurated, pinkish lesions, and central necrosis and crusting occur in those resulting from the more concentrated mixtures On the eighth day a record is made of the size of the papules and the area of necrosis by tracing on transparent paper Tests with at least four serums and a control (twenty injections) can be accommodated on a single rabbit of ordinary size

*Interpretation of Results*—The serums are classified according to the degree of inhibition in the size of the test serum lesions and areas of necrosis as compared with the control lesions on the same rabbit As indicated by Sabin, significant lesions are produced at the inoculated areas on almost all rabbits with the 1 20,

TABLE 3—Conditions with Which All Neutralization Tests Gave Negative Results

	Number of Serums Tested
A Congenital	
Macular degeneration	2
Optic nerve atrophy	3
Cataracts	2
Persistent tunica vasculosa lentis	1
Coloboma of iris	1
B Congenital or acquired	
Retinitis pigmentosa	1
Retinal hemangioma	1
C Acquired	
Keratitis	5
Inflammatory retinal detachment	2
Retinitis proliferans	1
Intraocular hemorrhage	1

1 100 and 1 1,000 dilutions, but much less regularly with the 1 10,000 dilution, of the control mixtures The last dilution was therefore omitted in 104 tests Table 1, after Sabin,<sup>19</sup> contains the criteria used for interpretation of results in these tests

#### RESULTS

The results of neutralization tests on all types of serums are given in tables 2 and 3

The data in tables 2 and 3 lend themselves to comparison only in relation to the criteria used. For example, Cowen, Wolf and Paige<sup>14</sup> use six dilutions of the suspension of toxoplasmas between 1:20 and 1:1,600, this would enable the observer to note the point at which small differences between the test serum lesions and the control lesions occur. These investigators

give "negative," "moderately positive," "doubtful" and "positive." In all probability there is general agreement among different observers as to the criteria for positive neutralization, the apparent differences being in the classification of serums in which the results are indecisive.

If equivocal results are considered to represent moderate neutralization, it can be stated that in

TABLE 4—Data in Cases of Congenital Chorioretinitis\*

Case No.	Patient	Age	Color	Sex	Microph. thalmos	Nystagmus	Squint	Relative Size of Lesions Yielded by Serum Toxoplasma Mixtures				Classification
								1:20	1:100	1:1,000	1:10,000	
1	R S	6 mo	W	F	—	+	+	++	++	—	—	Positive
2	R B	7 yr	W	M	+	+	+	+++	++	—	—	Positive
3	N T	11 mo	W	F	—	?	?	+++	++	—	—	Positive
4	L H	1 mo	N	M	+	?	?	+++	++	—	—	Positive
5	B H†	1 mo	N	M	+	?	?	++++	++++	+	—	Negative
6	M R	17 mo	W	M	—	+	+	++++	++++	++	+	Negative
7	D M	21 mo	W	M	—	+	+	++++	++++	+++	+	Negative
8	B J	9 mo	W	F	—	+	+	+++	++	—	—	Positive
9	A B	7 yr	W	F	—	+	+	++++	++++	++	—	Equivocal
10	C S	9 mo	W	F	+	+	+	++++	++++	+++	—	Negative
11	L H	7 yr	W	F	+	+	+	++	++	—	—	Positive
12	J C	20 yr	W	M	—	+	+	++++	+++	+	—	Equivocal
13	J B	21 yr	W	F	—	+	+	++++	+++	+	—	Equivocal
14	W M	21 yr	W	M	—	+	+	++++	++++	+++	++	Negative
15	T W	10 yr	W	F	—	+	+	++	—	—	—	Strong positive
16	A S	15 yr	W	M	+	+	+	++++	++	—	—	Positive
17	L S	22 yr	W	F	—	+	+	++	++	—	—	Positive
18	E S	16 yr	W	M	—	+	+	++++	++++	++	—	Negative
19	M H	14 yr	N	F	—	+	+	++++	+++	++	—	Equivocal
20	J M	15 yr	N	M	—	+	+	++++	+++	++	—	Equivocal
21	J O	13 yr	W	M	—	+	+	++++	++	—	—	Positive
22	B M	14 yr	W	F	+	+	+	++++	++++	++	—	Negative
23	T H	16 yr	N	F	—	+	+	++++	++++	+++	+	Negative
24	A B	23 yr	W	F	—	+	+	++++	++++	+++	+	Negative
25	G S	16 yr	W	F	—	+	+	++++	++++	++	+	Negative
26	R M	25 yr	W	M	—	+	+	++++	+++	+	—	Equivocal
27	S J	8 yr	W	M	—	+	+	+++	++	—	—	Positive

\* In this table, and in tables 5, 8 and 9, + indicates that the sign was present or that the reaction was positive, —, that the sign was absent or that the reaction was negative, ?, that information was not available and —, that the control lesion was inadequate for comparison or that no injection was made.

† The initial "B" is meant to represent "baby," since the infant was not named.

TABLE 5—Results for Parents of Patients with Congenital Chorioretinitis

Patient's No. in Table 4	Patient	Parent	Relative Size of Lesions Yielded by Serum Toxoplasma Mixtures				Classification
			1:20	1:100	1:1,000	1:10,000	
1	R S	Mother	+++	++	—	—	Positive
1	R S	Father	++++	++++	+++	—	Negative
2	R B	Mother	+++	++	—	—	Positive
3	N T	Mother	+++	+	—	—	Positive
4	L H	Mother	++	—	—	—	Strong positive
5	B H	Mother	++	—	—	—	Strong positive
7	D M	Mother	++++	++++	+++	+	Negative
7	D M	Father	++++	+++	++	—	Equivocal
8	B J	Mother	++++	+++	++	—	Equivocal
27	S J	Mother	+++	++	—	—	Positive

also use, in addition to buffered saline solution, normal serums as controls. The serums are classified as "positive" when the test serum lesions and the central areas of necrosis are in general one-half or less the size of the control lesions and are entirely inhibited in the higher dilutions of the suspension of toxoplasmas at which control lesions still appear, and as "suggestively positive" when the differences are distinct but less pronounced. When the contrast is minor or absent, the result is termed "doubtful" or "negative." The formulas used in Crother's series of tests were not given, although the results were designated as "strongly positive," "posi-

63 per cent of the cases of congenital chorioretinitis in which Toxoplasma might be suspected as an etiologic factor strong to moderate neutralization was obtained. It is interesting that the incidence of positive or equivocal results in patients with acquired chorioretinitis or anterior uveitis and in normal persons, exclusive of parents of infants or children with congenital chorioretinitis, was in the range of 10 per cent, which may represent the margin of error. While the per cent of parents, especially mothers, with antibodies was high, the number tested was too small to have a statistical value. The incidence of positive and equivocal results in the series



as a whole, 211 subjects, was 12 and 8 per cent respectively. The serums of 37 persons, or 22 per cent of those in the negative group, yielded a variable degree of neutralization in the 1:1,000 dilution of the *Toxoplasma* suspension, and in the 1:10,000 dilution when this was used. Sabin<sup>19</sup> obtained positive results with the serums of 39 per cent of 159 selected persons, but he did not state the number of equivocal results, if any, which were obtained.

macula was involved there was a temporal pallor of the disk. All lesions were inactive at the time of the test except those in one eye each in cases 12, 14 and 15.

Complete physical examinations and studies of the blood and the spinal fluid were performed on all infants. Serologic tests for syphilis were done in all cases and roentgenograms of the skull obtained in all cases except 9, 11 and 15. The patient in case 23 had congenital syphilis, and this was the probable cause of the chorioretinitis.

There were 5 cases of congenital chorioretinitis in which *Toxoplasma* antibodies were present and in which

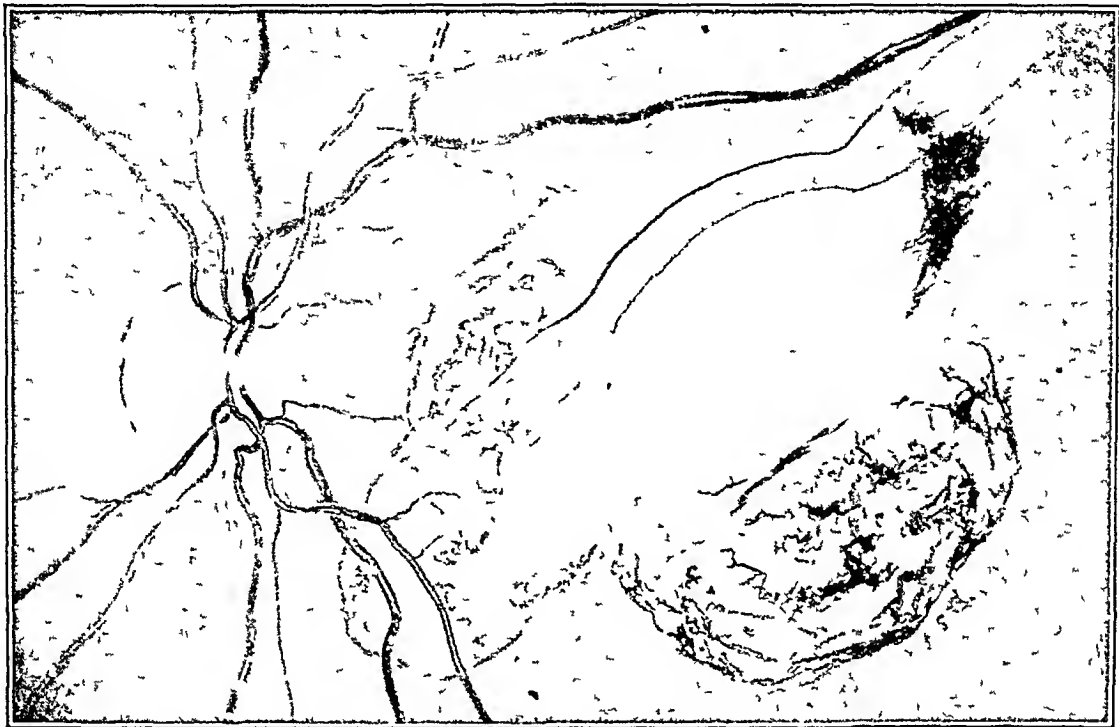


Fig. 4 (case 1, table 6)—Fundus of the left eye

The data in all cases of congenital chorioretinitis are shown in table 4.

The data on all parents of patients with congenital chorioretinitis whose serum was tested are shown in table 5.

TABLE 6—Cases in Which Positive Signs of Toxoplasmosis Were Associated with *Toxoplasma* Antibodies

Case No.	Patient	Age	Findings	Result of Test
1	R. S.	6 mo.	Cerebral calcification	Positive
2	R. B.	7 yr.	Cerebral calcification	Positive
3	N. T.	11 mo.	Convulsions, cerebral ventricular dilatation	Positive
4	M. H.	15 yr.	Cerebral calcification	Equivocal
5	L. H.	1 mo.	Cerebral calcification	Positive

*Cases in Table 4*—The presence of chorioretinitis was established before the age of 2 years in the first 12 cases, while in the remaining 15 there was a history of ocular symptoms or signs from infancy. The chorioretinitis was unilateral in case 13, information on this point was uncertain in case 5 and the condition was bilateral in all of the rest. There was macular involvement in all eyes except those in case 10 and one eye each in cases 12 and 15. In all cases in which the

the diagnosis of toxoplasmosis was supported by other clinical manifestation, as shown in table 6.

*Cases in Table 6*—CASE 1—R. S. had had poor vision and crossed eyes from birth. There was a history of difficulty in feeding and a generalized cutaneous eruption in early infancy. Slight eosinophilia was found on the child's admission to the hospital at 6 months of age. These features have been described occasionally in cases of infantile toxoplasmosis.<sup>14</sup> The results of examination of the cerebrospinal fluid, including animal inoculations, were entirely negative for *Toxoplasma*. The patient was readmitted to the hospital at 16 months of age with convulsions and fever, which followed an attack of otitis media. *Pneumococcus* type XII was cultured from the cerebrospinal fluid, and the symptoms quickly subsided on combined penicillin and sulfadiazine therapy. The child is 24 months old at the time of this report and is slightly retarded mentally. Ophthalmoscopic examination showed that the media of the left eye were clear. In the macular region there was a large healed chorioretinal lesion, in the center of which was a blue-green, egg-shaped elevation of the retina, with fibrous attachments extending into the vitreous. The disk was yellow-white. The remainder of the fundus was normal. A picture of the left fundus is shown in figure 4. The fundus of the right eye was obscured by a heavy sheet of fibrous tissue, which extended to the back of the lens. There

was a macular lesion, similar to that found in the left eye. The cerebral calcification is shown in figure 5.



Fig 5 (case 1, table 6) —Roentgenogram of the skull, showing areas of cerebral calcification

congenital pyloric stenosis. Vomiting continued for several months. The convulsions, which were present at 11 months of age, consisted of spasmodic twitchings of the arms and legs associated with a sharp cry. At the time of the serologic test the spinal fluid was clear, colorless and under normal pressure, with 3 lymphocytes per cubic millimeter and 146 mg of protein per hundred cubic centimeters. Organisms resembling those shown in figure 1 were seen with Wright's stain of the spinal fluid, but, unfortunately, the slide was broken before photographs could be obtained. Inoculation of this fluid into mice and guinea pigs was without results. The chorioretinitis was of the disseminated circumscribed type.

CASE 4—An early history was not obtained in the case of M. H. In the left eye there was a chorioretinal lesion, similar to that shown in figure 6. An identical lesion had been described earlier in the right eye, but at the time of the examination the pupil on this side was occluded, as a result of later inflammation.

CASE 5—L. H. exhibited uveokeratitis at 1 month and cerebral calcification at 2½ months of age. The eyes were microphthalmic, but the fundi were not seen until the infant was 5 months old, when bilateral macular chorioretinitis was found.



Fig 6 (case 2, table 6) —Fundus of the left eye

CASE 2—R. B. had microphthalmos, healed bilateral macular lesions and cerebral calcification at the age of 2 years. When he was reexamined at 7 years of age, the right pupil was almost occluded by adhesions of the iris to a cataractous lens, and vision was reduced to the barest perception of light. Ophthalmoscopic examination of the left eye revealed a large, oval, inactive, sharply margined chorioretinal lesion in the macula. The temporal portion of the disk was covered by a veil of glial tissue, which extended fanlike for a short distance and gradually blended with the normal retina on that side. The retinal arteries were moderately narrowed. Figure 6 shows the left fundus. The early description of the lesion in the right macula corresponded to that of the lesion in the left eye. Figure 7 shows the cerebral calcification. The cerebral condition shows no conspicuous change from that found at 2 years of age.

CASE 3—N. T. had convulsions from the sixth day of life. Projectile vomiting commenced on the fourteenth day, at which time the patient underwent operation at another hospital on the basis of a diagnosis of



Fig 7 (case 2, table 6) —Roentgenogram of the skull, showing multiple areas of cerebral calcification

The diagnosis of toxoplasmosis was proved or was considered probable in 4 other cases in which there were congenital chorioretinitis and other evidence of the disease. The serologic tests gave negative results. These cases are included in table 7.

TABLE 7—Cases in Which Positive Signs of Toxoplasmosis Were Associated with Negative Results of Neutralization Tests

Case No.	Patient	Age at Time of Test	Findings
1	B H	1 mo	Parasitic cysts in tissues of central nervous system and eye at autopsy
2	D M	17 mo	Hydrocephalus, psychomotor retardation
3	M R	21 mo	Convulsions, dilatation of cerebral ventricles
4	E S	16 yr	Hydrocephalus

Cases in Table 7—The serums of B H, case 1, table 7, and L H, case 5, table 6, who were identical twins, and the serum of their mother were furnished by Dr



Fig 8 (case 4, table 7)—Roentgenogram of the skull, showing elongation in the anteroposterior diameter, irregular areas of rarefaction of the inner tables of the cranial bones and widening of the sella, associated with hydrocephalus.

W W Zuelzer<sup>25</sup> who has described the clinical and pathologic aspects of these cases. The lesions in the eyes are to be the subject of a separate report by Zuelzer. Iridocyclitis and macular chorioretinitis with toxoplasmas in the lesions were found in the right eye of B H at autopsy. The serum was obtained twelve hours post mortem and dried from the frozen state twenty-four hours later. The result of the test on this serum was reported as "doubtful," since it neutralized the 1:1,000 and 1:10,000 dilutions of the suspension of toxoplasmas, but it is included in the negative group because it was inactive against the 1:100 dilution. It is possible that the delay in obtaining and preserving the serum may have been responsible for the weak neutralization in this case, although positive results have been obtained with serum which had been en route in the mail for seventy-two hours or more in the unpreserved state.

D M, case 2, exhibited a maculopapular eruption and spasticity of the arms and legs from the sixth month of life. The results of studies of the blood and spinal

fluid, including animal inoculations, were entirely negative for Toxoplasma.

The seizures of M R, case 3, consisted of spasmodic contractions of the arms and legs and twitches of the face, which commenced at the age of 6 months. On the child's admission to the hospital, at 17 months of age, the white blood cell count was 16,300, with 60 per cent lymphocytes. The spinal fluid was normal.

E S, case 4, had convulsions during the first year of infancy. Evidence of long-standing hydrocephalus is shown in figure 8.

The last 3 patients were greatly retarded in mental development. D M and M R (cases 2 and 3) had disseminated circumscribed chorioretinal lesions, while the lesions in the eyes of E S (case 4) were identical with the condition shown in figure 6.

Seven cases of congenital chorioretinitis included in tables 4, 6 and 7 were from the Maryland School for Blind Children. The serum was positive for Toxoplasma in 1 case, equivocal in 2 cases and negative in 4 cases. One patient, M H, table 6, whose serum yielded an equivocal result had cerebral calcification, while another, E S, table 7, whose serum gave a negative reaction, had hydrocephalus (fig 8). It is probable, therefore, that Toxoplasma is an etiologic factor of some importance in the blindness due to congenital chorioretinitis found in institutions of this kind.

Neutralizing antibodies have not been consistently demonstrated by other investigators in all patients with proved or probable toxoplasmosis or in patients suspected of having the disease. Sabin<sup>15</sup> obtained a negative result with the serum of a boy with encephalitis from whose spinal fluid toxoplasmas were isolated by inoculation of guinea pigs. The serum of a 14 month old infant with convulsions, microcephaly, chorioretinitis, cerebral calcification and psychomotor disturbance, described by Levin and Moore,<sup>25</sup> and that of his mother were also found negative for neutralizing antibodies<sup>26</sup> by Sabin.<sup>15</sup> In 2 other patients in the series of the same author<sup>19</sup> with some of the clinical manifestations of toxoplasmosis, including cerebral calcification or chorioretinitis, antibodies were not found in the serum. There were also 9 of 10 infants or children with histories of convulsions beginning soon after birth, psychomotor retardation or palsies not associated with cerebral calcification or chorioretinitis who were without antibodies. In another of Sabin's<sup>15</sup> patients, already mentioned, who presented chorioretinitis, hydrocephalus, cerebral calcification and psychomotor retardation the serum showed only slight evidence

25 Levin, P M, and Moore, H. Fetal Toxoplasmic Encephalitis. A Type of Congenital Cerebral Disease, *J Pediat* 21: 673-679 (Nov.) 1942.

26 Complement-fixing antibodies were demonstrated

of neutralization at the age of 6 months, but there was an increase in neutralizing antibodies in subsequent months

The data in the 12 cases of acquired anterior or posterior uveitis in which positive or equivocal results were obtained are given in table 8

*Cases in Table 8*—The ocular lesions in all patients were in the active stage at the time of the test, although some of the patients had a history or clinical evidence of previous inflammation in the same or in the other eye. Some of the patients in the group were hypersensitive to tuberculin, others had blood agglutinins for Brucella or the complement fixation test gave a positive reaction for gonococci, several had chronic tonsillitis or sinusitis, and 1 had syphilis

infants in all cases were normal and remained so during an observation period of ten months. The serums of 3 patients which were tested had no antibodies. Also, the previous offspring of all the women had been normal. There were 6 other obstetric patients, without postpartum infection, whose serums were negative. It seems unlikely that 5 patients taken at random from a single ward would have latent toxoplasmosis with specific antibodies whereas patients with definite clinical evidence of the disease were without them. The impression is, therefore, that the antibodies in at least some of these patients were nonspecific

TABLE 8—Cases of Acquired Uveitis Associated with Toxoplasma-Neutralizing Antibodies

Patient	Color	Sex	Age, Yr	Diagnosis	Relative Size of Lesions Yielded by Serum Toxoplasma Mixtures				Classification
					1:20	1:100	1:1,000	1:10,000	
R J	W	F	35	Posterior uveitis	+++	++	—	—	Positive
N S	W	M	11	Posterior uveitis	++++	++	—	—	Positive
H C	W	M	10	Posterior uveitis	++++	++	—	—	Positive
I M	W	M	20	Posterior uveitis	+++	++	—	—	Positive
M P	W	F	20	Posterior uveitis	++++	++	—	—	Positive
J I	W	M	32	Posterior uveitis	++++	+++	+	—	Liquivocal
J P	W	M	29	Anterior uveitis	+++	++	—	—	Positive
G B	N	M	35	Anterior uveitis	++++	+++	+	—	Liquivocal
O S	W	M	30	Posterior uveitis	++++	+++	+	—	Liquivocal
R P	W	F	36	Anterior uveitis	++++	+++	++	—	Liquivocal
C B	W	M	57	Anterior uveitis	++++	+++	++	—	Liquivocal
I P	W	F	35	Posterior uveitis	++++	+++	++	—	Liquivocal

TABLE 9—Normal Persons Whose Serum Neutralized Toxoplasma

Patient	Race	Sex	Age	Relative Size of Lesions Yielded by Serum Toxoplasma Mixtures				Classification
				1:20	1:100	1:1,000	1:10,000	
F J	N	F	17	+++	++	—	—	Positive
C K	N	F	21	++++	++	—	—	Positive
G T	N	F	19	++++	++	—	—	Positive
C W	W	F	17	++++	+++	++	—	Liquivocal
M B	N	F	18	++++	+++	++	—	Liquivocal
L M	N	F	20	++++	++	—	—	Positive

Particular mention should be made of R J, who is also included among the parents in table 5 and who is the mother of patient 27 in table 4, her serum also yielded a positive reaction. She had a unilateral, round, nonpigmented, grayish white, slightly elevated macular lesion, 1 disk diameter in size. On one occasion posterior corneal precipitates and an aqueous flare were noted in the same eye. Except for pronounced sensitivity of the skin to tuberculin, a complete clinical survey revealed nothing abnormal.

The data for the normal subjects, other than parents of patients with congenital chorioretinitis, whose serums gave a positive or an equivocal reaction for Toxoplasma are shown in table 9.

The reason for the positive results in these cases is not clear. It is notable, however, that 5 of the 6 persons tested were Negro women in the maternity ward, all being tested ten days post partum. One of these patients had preeclampsia, while 3 had had postpartum infections, with moderate to high temperatures. The

#### NONSPECIFIC SERUM REACTIONS

In the group of cases of congenital chorioretinitis in which there was definite reason to suspect Toxoplasma as the etiologic agent, the incidence of positive or equivocal reactions was 63 per cent. From these results it would appear that a positive reaction in congenital chorioretinitis has definite diagnostic value. In the other groups, such as those cases of acquired anterior or posterior uveitis, and in normal persons antibodies were present in 10 to 14 per cent. On the other hand, negative reactions were obtained in 4 cases in which the diagnosis of toxoplasmosis appeared certain. An attempt was therefore made to find an explanation for the paradox of positive reactions in normal persons and negative reactions in the presence of disease, and to determine the conditions under which nonspecific neutralization of Toxoplasma, as suggested by the foregoing data, might occur.

The method used was that indicated by the results of the investigations of Sabin and Ruchman.<sup>27</sup> These authors observed that the neutralizing antibody appeared in rhesus monkeys as early as two weeks after infection and per-

<sup>27</sup> Sabin, A. B., and Ruchman, I. Characteristics of the Toxoplasma Neutralizing Antibody, *Proc Soc Exper Biol & Med* 51:1-6 (Oct) 1941.

sisted throughout the period of observation (fourteen months) without evidence of a persistent infection. The antibody was of low titer and was destroyed in serum exposed to a temperature of 56 C for thirty minutes. The neutralizing antibody which was present in the serum of an infant with congenital toxoplasmosis was similarly found to be thermolabile and of apparently low titer. The authors further described the results in neutralization that they had obtained with "hyperimmune" monkey serum, which was prepared by pooling the serum of monkeys repeatedly inoculated with *Toxoplasma*-infected tissues. This serum, which had originally yielded the low titer neutralizing antibody, after inter-

one to four weeks, unheated serum still gave either positive or equivocal reactions. However, tests performed with unheated and heated portions of serums which were obtained nine to

TABLE 10—Cases in Which the Serum Was Tested for Thermalability of the Antibody

Patient	Age	Positive Findings	Reaction of Serum	
			Portion Unheated	Portion Heated at 56 C
R S	15 mo	Congenital chorioretinitis, cerebral calcification	+	—
L H	1 mo	Congenital uveokeratitis, cerebral calcification	+	—
R B	7 yr	Congenital chorioretinitis, cerebral calcification	+	—
L S	23 yr	Congenital chorioretinitis	+	—

TABLE 11—Cases in Which Original Unheated Serum Gave a Positive Reaction and Both Heated and Unheated Portions Gave Negative Reactions Several Months Later

Patient	Age	Clinical Findings	Original Specimen II Unheated	Interval Between Venipunctures	Specimen III Unheated	Specimen III Heated, 56 C
E M	20 yr	Acquired posterior uveitis	+	17 mo.	—	—
J P	29 yr	Acquired anterior uveitis	+	21 mo	—	—
G T	19 yr	Normal	±	9 mo	—	—
O K	21 yr	Normal	±	9 mo	—	—

\* In this table, and in table 12, + indicates a positive reaction, ±, an equivocal result, and — a negative reaction

TABLE 12—Cases in Which Original Unheated Serum Gave an Equivocal Reaction and Both Heated and Unheated Portions Gave Negative Reactions Three Weeks and Ten Months Later

Patient	Age	Clinical Findings	Original Specimen I Unheated	Interval Between Venipunctures	Specimen II Unheated	Specimen II Heated, 56 C
J C	20 yr	Congenital chorioretinitis	±	10 mo	—	—
O W	18 yr	Normal	±	3 wk	—	—

vals of four and seven years' storage in an ordinary refrigerator was found to have a high titer antibody, which was not destroyed by heating the serum at 56 C for one-half hour. They concluded that this thermostable "hyperimmune" reaction was not due to the regular neutralizing antibody. The following measures were carried out to determine, if possible, the specificity of the neutralizing antibody according to the method suggested by the aforementioned authors. A number of serums were divided into two portions, and one part was tested in its natural state and the other after being heated at 56 C for thirty minutes. Table 10 shows the results in 4 cases, in all of which the unheated portion of serum gave positive results and the heated portion negative results, and confirms the observations of Sabin and Ruchman on the thermolability of the regular, low titer neutralizing antibody. Table 11 shows the results in 4 cases in which the unheated serum had formerly yielded at least one positive reaction. When retested in from

twenty-one months later gave negative results in all cases. Table 12 shows 2 other cases in which equivocal results were obtained with the original unheated serum and in which negative results were obtained with both the unheated and the heated portion of the serum obtained three weeks and ten months later. An analysis of the results of this small number of cases shows that in all cases the antibody was of low titer and probably the same. In the 6 cases shown in tables 11 and 12 the antibody disappeared spontaneously in a period of three weeks to twenty-one months. This, however, was not a uniform phenomenon, since in 3 cases of congenital chorioretinitis not shown in table form the antibody was still present nine to fifteen months after the original positive test. The fact that the results of the test can be reproduced with remarkable precision with preserved portions of the same specimen of serum whereas the differences are noted with serum which is obtained later suggests that the variable factor in neutralization is humoral in origin.

Since a variable antibody content of the serum was demonstrated in 4 persons, table 11, with elevated temperature, spontaneous in 2 patients with postpartum infections and induced by means of intravenous administration of typhoid vaccine in 2 others with acquired uveitis, fever as a possible cause of nonspecific antibody production is suggested. However, similar observations were made on 2 other persons, table 12, with normal temperatures, 1 of whom had chorioretinitis from the fourth month of life. In the patient last mentioned there was evidence of a reactivated chorioretinal lesion in one eye at the time of the original test. Summing up the results in the cases in tables 10, 11 and 12, it would appear, first, that the low titer neutralizing antibody is thermolabile and, second, that there is a tendency for it to disappear spontaneously from the blood serum. This observation would explain the negative results obtained in the 4 cases of congenital toxoplasmosis, although an alternative possibility, as suggested by Sabin,<sup>13</sup> is that the antibody may not be produced early in all instances. It is evident that in some cases the antibody may persist for many months, or even years. However, there is no definite explanation for what appear to be false positive reactions. In this series the high titer, thermostable neutralizing antibody described by Sabin and Ruchman as occurring in "hyperimmune" monkey serum was not found in any human serums, although a potent neutralizing antibody which was not inactivated at a temperature of 56 C for thirty minutes was found in the serum of immune rabbits. This study, therefore, does not support the implication which follows from the results of the investigations of these authors that the nonspecific antibody would be thermostable. It does suggest, though, that nonspecific serum reactions might occur in 10 to 14 per cent of persons without clinical evidence of toxoplasmosis as it is at present understood.

Other possible factors which might cause a nonspecific serum response were investigated. It seemed possible that a variation in the  $p_H$  of the saline diluent for the suspension of toxoplasmas might be a responsible factor. Accordingly, 2 serums which had been positive ten and twenty-one months previously were retested, using diluents of varying  $p_H$  between 5.9 and 7.5. Unfortunately, all of these tests gave negative results, the antibody having spontaneously disappeared, so there is no information available on this point.

The possibility that the results might be influenced by the difference in the strains of *Toxoplasma* was considered. However, in many cases the variation in results occurred with the same strain, and there were 3 serums in the group which neutralized both strains of *Toxoplasma*. Moreover, monkey serum<sup>28</sup> which came from monkeys infected with one strain neutralized both strains of *Toxoplasma*. Therefore there is no evidence from this study that the strain of organisms used in the test would affect the results.

#### SUMMARY AND CONCLUSIONS

Strong to moderate neutralization of *Toxoplasma* was obtained with the serum of 63 per cent of 27 patients with congenital chorioretinitis, 14 per cent of 97 patients with anterior or posterior uveitis and 10 per cent of 58 normal persons other than the parents of infants or children with congenital chorioretinitis. Of 9 patients with congenital chorioretinitis and other evidence of toxoplasmosis only 5 had antibodies. Antibodies were present in 6 of 7 mothers of patients with congenital chorioretinitis. Therefore it would appear that the demonstration of the neutralizing antibody should be considered a factor of moderate diagnostic value only in patients with congenital chorioretinitis. Its absence from serum does not rule out the possibility of toxoplasmic infection.

The neutralizing antibody is of low titer, is thermolabile and shows a tendency to disappear from the blood serum in a few weeks, although it may persist for fifteen months or longer, possibly even indefinitely in some cases. Aside from possible instances of familial infection, *Toxoplasma*-neutralizing antibodies may be demonstrated in 10 to 14 per cent of persons without clinical manifestations of toxoplasmosis as the disease is at present understood. It is probable that at least in some of these persons the antibodies are nonspecific.

Dr. Edwards A. Park, director of the department of pediatrics of the Johns Hopkins Medical School, permitted the study of various patients in his services and offered laboratory facilities at the Harriet Lane Home. Dr. W. W. Zuelzer, of the Children's Hospital of Michigan, furnished the serums and the histories in his cases. Major A. B. Sabin, formerly of the Children's Hospital of Cincinnati, and Dr. A. Wolf, of Columbia University College of Physicians and Surgeons, furnished the strains of *Toxoplasma* used. Major A. B. Sabin gave a generous supply of *Toxoplasma*-immune monkey serum, and Miss Helen Zepp and Miss Elizabeth Fisher assisted in the details of the laboratory technique.

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28 Serum supplied by Major A. B. Sabin



# Ophthalmologic Reviews

EDITED BY FRANCIS HEED ADLER

## HERPES ZOSTER OPHTHALMICUS

REPORT OF CASES AND REVIEW OF LITERATURE

AMBROSE EARL EDGERTON, M D

SAN FRANCISCO

Herpes zoster ophthalmicus presents an interesting problem. Although the disease was known to physicians of antiquity, their ideas concerning the disorder were obscure. They described, in considerable detail, the characteristics of the disease, but their interpretations were brief. The disease was known as zoster to the Greeks, and Pliny, a Roman, is said to have been the first to apply to the eruption the denomination of zona. From these ancient times to the early nineteenth century the literature is scant on the subject. Mahlis, in 1818 suggested that the eruption of herpes zoster followed the distribution of nerves, and Parrot, in 1856, noted that the eruption like pain developed along the course of branches of nerves, most frequently superficial, and that it was here that the neuralgias ordinarily manifested themselves. This was proved in 1861 by von Barenprung. Hutchinson in 1866, and Bowman, in 1867, were the first to describe herpes zoster ophthalmicus in detail and each reported several cases.

An enormous amount of work has been done in recent years in the investigation of the pathology, treatment and various manifestations of zoster and other herpetic diseases. Although the condition is comparatively rare, the literature on this subject is large, a great many cases having been reported.

Herpes zoster has been noted to occur in the proportion of 1 to 2 per cent of all diseases of the skin. Horner found 2 instances in 28,328 cases of cutaneous disease during a six year period. Joseph found 163 cases of herpes zoster in 15,603 cases of diseases of the skin. Knowles, 286 cases in 21,337 cases and Greenough, 235 cases in 17,741 cases. Fouchard in 1898, found 57 cases of ophthalmic zoster in 5,000 cases of diseases of the eye. Da Fonseca, in 1882, saw 4 cases of ophthalmic zoster in 13,000 cases of ophthalmic disease, and Galezowski encountered 19 cases among 36,000 cases of diseases of the eye. Head and

Campbell found 18 cases of the ophthalmic form in 416 cases of herpes zoster. Berggreen and Schuler, in 1938, reported 2,014 cases of herpes zoster occurring in Berlin in 16 of which the fifth nerve was involved. Schonfeld encountered disturbances of ocular innervation in 12 per cent of cases. Only 5 cases were seen at the Wills Hospital in 1913-1914, out of a total of 30,000 cases of ocular disease.

Laqueur, in 1870, had found 52 instances of ophthalmic zoster in the literature, and Armaignac, in 1884, observed that a total of 200 cases had been reported. There are several varieties, distinguished mainly by the region involved. In 1924 Achard stated that cases of the ophthalmic type represented about 7 per cent of the cases of all types of herpes zoster. Ophthalmic zoster is, after thoracic zoster, the most frequent type, and, like the diseases in other localizations it is usually unilateral and nonrelapsing. At times its frequency amounts to an epidemic, as reported by Head and Campbell, Trousseau, and Levaditi and at other times it is seldom seen. Various manifestations of the disease are continually being reported, but little is definitely known. Theories regarding its cause are frequently being advanced but the etiologic factors are still obscure.

The disease may be of long duration, the period ranging from two weeks to several months, and occurs with greatest frequency and with most severity in the latter half of life. It displays no predilection for age, color or sex. It may be confined to certain branches of the fifth nerve, and it is observed most frequently on the inner half of the upper lid, the adjacent side of the nose, over the eyebrow and in the region of distribution of the supratrochlear, the infratrochlear, the supraorbital and the oculonasal nerve. The area most frequently affected is that of the supraorbital nerve, the lesions often exhibiting a symmetric design along various ascending and descending branches of this nerve, and next in frequency is the area of the supratrochlear nerve. The frontal nerve may be affected alone and

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some believe that this nerve is always involved. Rossander, in 1877, described a case, however, in which only the infratrochlear nerve was affected. The disease may be localized along the lacrimotemporal nerve and involve the temple. The more serious complications occur when the lacrimal and nasociliary branches are affected. The entire territory of the ophthalmic nerve may be involved—namely, the upper lid, which is swollen and covers the globe, the internal frontal region, on which are distributed the vertical rows of vesicles, arranged in the form of a fan, and the anterior third of the scalp and the foot of the nose. Sometimes a single branch is affected—for example, the frontal, causing involvement of a large triangular territory with a superior base, or the nasal branch, resulting in involvement of the internal third of the upper lid and the ala nasi, or the lacrimal branch, with consequent implication of the external third of the eyelid. Bar, in 1925, reported a case, from which he drew interesting deductions. In addition to cutaneous anesthesia in the frontal region, the upper lid, the conjunctiva and the cornea, on the right side, there was involvement of the ophthalmic division of the fifth nerve with the exception of the terminal branches of the nasociliary and anterior ethmoidal nerves, resulting in diminution of sensation in the lower lid and the upper half of the side of the nose. From this derangement of sensibility, he concluded that twigs of the first division, as well as fibers from the second branch, of the fifth nerve supply the lower lid.

Herpes zoster ophthalmicus may be associated with zoster of the superior maxillary branch, with vesicles on the lower lid, the superior maxillary region as far as the upper lip and the malar bone, the tonsils and the velum palati, with zoster of the inferior maxillary branch, with vesicles on the chin and the lower lip, with geniculate zoster, with vesicles in the external auditory canal and frequently with facial paralysis, and with zoster of the glossopharyngeal nerve.

Sometimes all nerves of the first division, or several of these branches, are affected simultaneously with the second division. Involvement of all nerves of the first and second divisions of the nerve is less often seen, and involvement of all three divisions together is rare. Cases of zoster without eruption are exceptional, although Lederer, in 1900, reported such cases.

#### ANATOMIC RELATIONS OF THE FIFTH NERVE

The physiologic makeup of the fifth nerve is complicated. The trigeminal nerve resembles

a spinal nerve, being made up of a compressed group of afferent, posterior roots. Its ganglion, the gasserian, is a fusion of posterior root ganglions of all the posterior sensory roots, corresponding to all motor nerves from the brain stem. The nerve enters the pons midway between its lower and its upper border and sends an ascending root upward to the brain stem and a descending root to the tissues as far down as the second cervical level. Any pathologic process affecting the cells in the pons, such as meningitis, pontile tumor or inflammation, may be referred to the corresponding point of the peripheral distribution. In the main the nerve is sensory, with its center the gasserian ganglion, but it is linked up with fibers from the cervical portion of the sympathetic chain, which carry vasoconstrictor impulses and motor fibers to the levator palpebrae muscle, to Muller's muscle and to the fibers of the dilator pupillae.

The gasserian ganglion lies in the middle fossa of the skull, and from its upper portion arises the ophthalmic division of the fifth nerve, which passes into the cavernous sinus and runs along its lateral wall. The ophthalmic division gives off a branch to the tentorium, the recurrent nerve of Arnold, and sends filaments to the third and sixth nerves and sometimes to the fourth nerve. Involvement of this branch to the meninges may simulate symptoms of meningitis.

The ophthalmic division, the smallest of the three divisions of the fifth nerve, is a flat nerve, about 1 inch (2.5 cm) in length, and is purely sensory. It is joined by sympathetic fibers from the superior cervical ganglion, and just before entering the sphenoid fissure, it divides into the frontal, the lacrimal and the nasociliary nerve.

The eye receives its sensory innervation from the ophthalmic division of the fifth nerve. Afferent impulses pass by this route to the gasserian ganglion and then to the pons. Some fibers end in the chief sensory nucleus, and others descend through the pons and the medulla to the upper segments of the spinal cord. These form the spinal root of the fifth nerve and form connections with the substantia gelatinosa of Rolando, which extends from the pons to the upper cervical portion of the cord. From the sensory nuclei, a second afferent neuron decussates to form the trigeminal fillet and then passes to the optic thalamus, where a third afferent neuron passes by way of the internal capsule and the corona radiata to the cortex. Thus, the fifth nerve fibers are exposed to injury over a wide area.

The first branch, the ophthalmic nerve, with the ciliary ganglion, supplies sensation to the upper lid, the conjunctiva, the eyeball, the lac-



lacrimal gland, the forehead, the anterior part of the scalp, the frontal sinus, the root and anterior portion of the nose and the caruncle, and a branch from the ciliary ganglion enters the optic nerve with the central artery of the retina.

The second branch, the superior maxillary nerve with the sphenoid ganglion, furnishes sensation to the cheek, the anterior temporal region, the lower lid, the side of the nose, the upper lip, the upper teeth, the mucous membrane of the nose, the nasopharynx, the antrum, the ethmoid cells, the soft palate, the tonsils and the roof of the mouth.

\* The third branch, the inferior maxillary nerve, with the otic and submaxillary ganglions, is both motor and sensory and is distributed to the skin of the side of the head, part of the auricle and the external auditory meatus, the lower part of the face, the lower lip, the mucous membrane of the mouth, the tongue, the mastoid cells, the lower teeth, the gums, the salivary glands, the dura mater and the skull.

The frontal nerve is the longest branch of the ophthalmic nerve. It enters the orbit through the superior orbital fissure and divides into two branches, the supratrochlear and the supraorbital. The supratrochlear branch escapes from the orbit between the trochlea and the superior orbital foramen passing up to the forehead, and gives off branches to the conjunctiva and the skin of the upper lid. The supraorbital branch passes through the supraorbital foramen, giving off branches to the upper lid, and ends in two cutaneous branches to the scalp. The supraorbital branch is the nerve most often affected with herpes zoster, and next in frequency is the supratrochlear, yet the latter rarely suffers alone. These nerves supply the upper lid and forehead and may extend as far back as the vertex.

The lacrimal nerve is the smallest branch of the ophthalmic division. It anastomoses with the facial nerve (pars intermedia of Wrisberg) and passes into the orbit through the superior orbital fissure, enters the lacrimal gland and gives branches to the gland, the conjunctiva and the skin of the upper lid. It is often difficult to tell whether or not this nerve is involved in cases of herpes zoster if the conjunctiva and the upper lid are affected, because they receive filaments also from the superior trochlear, from the frontal and from the inferior trochlear nerve. The temporal branch of the superior maxillary nerve in its course through the orbit receives a filament from the lacrimal nerve, and at times the zygoma may show vesicles, although the superior maxillary nerve itself may not be involved.

The nasociliary nerve becomes the main sensory nerve to the eyeball. This nerve crosses the optic nerve, and at the inner wall of the orbit it divides into two terminal branches, the infratrochlear nerve and the nasal nerve proper, supplying the iris, the ciliary body and the choroid. The infratrochlear nerve emerges from the orbit above the internal tarsal ligament. Its branches supply the sac, the conjunctiva, the skin of the lids and the root of the nose. As far as the eye is concerned, the nasal nerve is the most important. The nasal nerve proper leaves the orbit by the anterior ethmoid foramen to enter the anterior part of the cranium, at the inner margin of the cribriform plate. Here it turns forward under the dura and passes through a narrow opening at the side of the crista galli to reach the nasal cavity. It passes below the lower margin of the nasal bone and gives off branches to the skin and makes connections with the facial nerve. In its course, it sends a branch to the ophthalmic ganglion, a small fragment running alongside the optic nerve. It gives off the long root of the ciliary ganglion, from which short ciliary nerves pass to the iris, then it sends long ciliary branches to the ciliary muscle and the iris, and subsequently divides into the external and the internal nasal nerve, which supply the middle and the tip of the nose.

This nerve exhibits a complex distribution. Through its ciliary ramifications it furnishes sensibility to the globe, through its external course it innervates the internal part of the two eyelids, the lacrimal sac and the nose. Its internal distribution is partly to the nasal mucosa and partly to the skin of the lobe of the nose. The ciliary, or lenticulate, ganglion lies in the orbital fat between the optic nerve and the external muscles. It is made up of a filament from the nasal branch of the ophthalmic (sensory) nerve, fibers from the oculomotor nerve and a branch from the cavernous plexus of the sympathetic chain. Its branches are the short ciliary nerves, which accompany the long ciliary nerves and pierce the sclera near the entrance of the optic nerve. The short ciliary nerves are distributed to the cornea, the iris and the ciliary body. Inflammation of the ganglion may bring about dilation of the pupil, with increased ocular tension, through its sympathetic fibers.

The posterior parts of the sclera are supplied from the ciliary nerves. Anteriorly, the ciliary nerves form a plexus, fibers from this area are distributed to the anterior part of the sclera, behind the sclerocorneal junction (limbus), and go forward to the sclera. The corneal nerves enter this structure at about the middle third

of its thickness. These fibers form an anastomosis at the limbus, where about sixty branches enter the cornea.

Thus, the upper lid and the conjunctiva receive their sensory nerve supply from several branches of the fifth nerve—the supraorbital, the frontal, the infratrochlear and the supratrochlear. The lacrimal nerve supplies the lateral angle of the eye. The conjunctiva of the bulb likewise shares in the nerves of the lids and also gets some supply from the lacrimal nerve. Small branches of the ciliary nerve also enter the conjunctiva, where they combine with other nerves in the form of a plexus and then distribute themselves partly in the conjunctiva and partly in the sclera.

Königstein expressed the belief that the epithelium of the cornea is supplied by nerves arising from the conjunctival plexus, the substantia propria, by the superficial branches, and Descemet's membrane and the cornea over it, by the deep ramifications. His investigations also showed that the portion of the corneal nerves originating in the conjunctival nerves were developed in proportion to the development of the conjunctival portion of the cornea. When there is complete development of the pars conjunctivalis of the cornea, the epithelium of the cornea is supplied solely by conjunctival nerves. In that case the scleral portion of the cornea has its own, independent plexus.

Anomalous ramifications and an unconventional distribution of branches of the fifth nerve have been reported in some cases, and this should be taken into consideration in any problematic case of herpes zoster ophthalmicus. Arnold observed that the lacrimal nerve arose from two roots, one having its origin in the supraorbital nerve and the other in the nasociliary nerve in some cases. Svitzer saw a branch of the lacrimal nerve enter the bulb through the sclera and observed the radix longa of the ciliary ganglion arising from the supraorbital nerve. Pye, Howse, Davies and Colley noted the radix longa arising from the lacrimal nerve. Supernumerary roots of the ganglion have been described by Hyrti, one such root which he observed separated from the lacrimal nerve and entered the ciliary ganglion.

## CLINICAL FEATURES

### INCIDENCE

*Age*—Apparently, in herpes zoster neither age nor sex assumes a decisive role, although it has been observed in children that pain is less severe, the course of the disease is shortened and symptoms of paralysis subside more readily. It is clear that observers are not agreed as to the time

in life when the disease is most prevalent. In 2,250 cases of herpes zoster ophthalmicus the average age was 44. The disease may occur at any age but is more commonly seen among elderly people. They are more prone to attack when their physical condition is lowered, and many cases have been reported in which the zoster followed a recent illness or operation. Lodge and Lodge, in 1923, reported 20 cases, in which the average age was 55. Stizenmund stated that the disease developed ordinarily in middle life, rarely in youth or infancy. Rayer claimed that the disease was more frequent in adults. Brissaud found that most patients were between 60 and 70 years of age. Elliot found the average age to be 41, and Hewlett, 48.

On the other hand, Fox claimed that the disease was common in the young. Evans found that one half of his patients were under 14 years of age. Bateman stated that the condition occurred most frequently between the ages of 12 and 25 years. Fagge and Pye Smith found 100 cases, in 46 of which the patient was under 20 years of age. Crocker reported that three fourths of the patients seen were under 13 years of age. Stelwagon noted that the disease was most frequent in persons between the ages of 10 and 30 years. Head reported 378 cases, in 283 of which the patient was under 25, with an average age of 12 years. Rollet, Bujadoux and Blanc, in 1931, described a case of the disease in a girl of 10 years, with involvement of all three branches of the nerve on the right side and associated paralysis of the ocular muscles. Muscular paralysis as a complication is rare in children. Cases of ophthalmic zoster in children have been reported by Ginestous, Agnello, Fisher, Lederer, Desobry, McMurray, Gallemaerts, Rollet and Bussy, Halipré, Roll, Jessop, Koch, Knox, Mayou, MacNab, Knowles, Rachmaninow and others. Bonar and Pearsall saw a case of the disease in an infant 4 days old, and Lomer cited 2 cases of Bohn's in which the disease occurred in infants 5 and 7 months of age. Kolb, in 1909, described a case of a disorder in a newborn infant in which multiple groups of scars were symmetrically arranged in the area of the first and second divisions of the fifth nerve; these lesions he considered the remains of a bilateral herpes zoster ophthalmicus present in intra-uterine life. There are apparently two periods in life in which herpes zoster is most likely to occur—under 14 and over 40 years of age.

*Sex*—Some authors report a predominance of zoster in males, others claim that a greater number of females are attacked, and some believe that males and females have the disease

with equal frequency. Lodge and Lodge found the incidence to be the same in the two sexes. Evans found that females had the disease more often than males, the incidence being 75 per cent. Hewlett observed more cases of zoster in females. In the fifth and sixth volumes of the reports of the Royal London Ophthalmic Hospital are described 51 cases, 31 of males and 20 of females. Head (cited by Romei, in 1910) stated that in the London General Hospital in one year herpes zoster occurred in about 1 of 500 cases. Of 378 cases of all types of the disease, males were affected in 240 and females in 138. Hybord reported that males were more often affected than females, and this opinion was concurred in by Jaksch, Koch, Laqueui, Pacton, Aubineau, Strzeminski and Disson. Cantonnet, in 1935, claimed that the disease affected males in three fourths of the cases and the left side in two thirds of the cases. Davidson found that 75 per cent of patients were males, Joseph, 70 per cent, Brissaud, 75 per cent, Knowles, 70 per cent, Greenough, 45 per cent, and Metz, 65 per cent. I found that males were affected in 54 per cent of 2,250 cases of herpes zoster ophthalmicus. The right eye was affected in 54 per cent of all cases.

*Seasonal Factors*—The seasonal occurrence varies. Many believe it to be associated with the cooler months of the year, but epidemics have occurred in the summer months as well. Neligan, in 1852, said that in the summer and autumn of some years the disease would appear to be epidemic among children. Paisons claimed that the disease had a definite seasonal incidence—in the spring and in the fall. Schamberg called attention to the predominance of cases in the spring and autumn. Brain claimed that the same seasonal incidence existed. Elliot, in 1918, reported 19 cases that occurred in India between September and March. Von Bokay, in Budapest, in 1928, reported more cases in December and January, about one month after the incidence of varicella had reached its peak. Knowles encountered the largest number of cases in July and August, while Stanford, Greenough, Blaschko, Joseph Head and Campbell reported the occurrence of more cases in the spring. Head stated the belief that the disease was associated with an atmospheric influence. Recent investigators claim that the disease is most frequent during October and November.

#### EXPOSURE

Many investigators believe that herpes zoster develops as the result of chilling of the body due to exposure to wind, cold and dampness. Paget

in 1866, reported a case in which the disease developed in a man aged 25 after exposure to severe cold. Three days after exposure an eruption appeared on the right side of the upper lip and nose and the right cheek, involving the first and second branches of the fifth nerve. Jeffries, in 1871, described 3 similar cases. Stieren reported 16 cases in 1906, in all of which there was a history of exposure to cold and dampness. He expressed the belief that the disease was due to climatic conditions and personal habits. Khinedinst, in 1918, cited 3 more cases in which the eruption followed exposure. Other cases in which there was a similar history have been described, among others, by Eyer, Hinde, R. F. Moore, Lagarde, DaFonseca, Hybord, Horstmann and Martin.

#### PRODROMAL SYMPTOMS

The general prodromal symptoms of malaise, headache, nausea, chills, fever and anorexia usually precede the eruption by several days. These symptoms are sometimes absent, the prodrome consisting merely of local pains and being characterized by unilateral neuralgia. The fever usually recedes at the time of the cutaneous eruption. Preliminary gastric disturbances are sometimes present and are due to existent relations between the trigeminal and the vagus nerve. The cutaneous temperature is increased on the affected side, with anesthesia of the surface of the skin. The flushing and redness of the skin is sufficient to raise the cutaneous temperature as was first reported by Horner, in 1871, and by Paton, in 1926. The latter found that the temperature of the affected side was about 2 degrees (F) higher than that on the other side, but that it fell as the condition subsided.

#### PAIN

The disease is accompanied with subjective symptoms, especially excruciating pains of neuralgic type along the entire ophthalmic branch of the trigeminal nerve, at times radiating to other branches as far as the occiput and preceding the eruption, as a rule, by hours or several days. This interval, Pickard and Montgomery asserted, represents the growth and spread of the virus along the nerves, which has not as yet reached the ganglion. The neuralgic pains manifest themselves in all degrees of intensity. Deep-seated, intermittent pains of definitely neuralgic type and of periodic character may exist with superficial distress provoked by irritation of the skin. The pain may assume the form, at times, of an exceedingly violent cephalalgia occasionally with

ocular, supraorbital, retro-orbital or oculotemporal pain. The severity of the pain and the extent of the lesion bear no relation to one another. The greatest pain often is experienced when the cutaneous lesion is but slightly evident. In some cases nothing seems to relieve the torture. Rea suggested that this refractory pain is probably due to a lesion in the pons, since cutting of the sensory root does not relieve the pain.

The whole cycle lasts several weeks. The pain continues throughout the course of the illness and may last for years in the graver forms of the disease. Occasionally exacerbations occur after the disappearance of the zoster, while at other times the attacks of pain gradually become less severe, in any event, the pain is distressing because of its tenacity and reacts profoundly on the general condition of the patient. In elderly people, the distress may end only with the termination of life. The continuous after-symptoms have sometimes led to suicide. Forget reported such a case. In the aged, the pain may lead to severe prostration, and it has been responsible for exhaustion and death as reported by Jeffries, in 1869 and by Doggart, in 1933. All authors agree that, after the eruption, pain is incontestably the most important symptom of the disease.

In most cases, after decrease in severity of the main symptoms, there is reduced sensitivity or a feeling of numbness over the affected areas for a long time. In some cases, even years after an attack, exposure to cold air, wind or rain produces a tingling sensation in the skin, and at times the most intractable postzosterian pains are observed. Rea reported the case of a man who suffered severely six months after an attack, and Miles described a case in which the pains were so violent that the patient had applied carriage varnish to the skin of the scalp. This caused severe dermatitis of the face and lids and the skin finally sloughed over the forehead to the pericranium. Some patients have pain with headache and vomiting, simulating the symptoms of meningitis. This may be due to involvement of the meningeal branch of the ophthalmic division, which sends filaments to the tentorium before the nerve reaches the sphenoid fissure.

Anesthesia of the cornea may also occur, and on this subjective basis of insensibility there may be superimposed persistent pains, often severe, especially during the first few days of the disease, and the pains may be particularly persistent in the aged. Herpes zoster in children is different from zoster in adults as far as pain is concerned. In the child the pain is less severe, rarely continuing beyond the period of eruption.

## VESICLES

Herpes zoster ophthalmicus is an infectious disease of the nervous system characterized by the appearance of erythematous plaques on an edematous area of the skin and followed by the formation of yellow vesicles discrete or in groups, along the terminal ramifications of the fifth nerve. In some cases the eruption may be extensive but never spreads beyond the median line. The vesicles vary in size, are irregular and may occur in small or large groups, which are scattered or confluent, with a tendency to coalesce. They may appear simultaneously or at different times, in the temporal region, the forehead, the scalp, the nose or the upper lid, and the eye itself may be involved. The vesicles at first contain a clear yellow fluid, which in a few days becomes cloudy. The erythema of the skin gradually disappears, and the vesicles soon become modified in character. They may become purulent or hemorrhagic, even gangrenous at times, in some cases resulting in extensive loss of the skin. This is probably due to the virus, with edema and swelling of the sensory nerve, to the severity of the disease or to secondary necrotizing infection, which in some cases may assume considerable importance.

As a rule, after a few weeks the vesicles dry up and leave a characteristic black crust, of irregular outline, which gradually falls off, leaving the skin in an anesthetic state and very tender. Scarring of the skin usually occurs, especially if the lesions have been hemorrhagic. The blebs leave indelible scars, characteristic, slightly depressed, pale, white cicatrices of the skin, and their typical distribution often renders possible a retrospective diagnosis of previous herpes zoster.

These erythematous plaques are essentially distinguished by the fact that their site corresponds to the cutaneous region of the fifth nerve. The disease is not always localized in the skin but may attack also the mucous membrane, that is, the nasal mucosa, resulting in mucopurulent coryza, or the ocular conjunctiva, causing redness and discharge. Lesions have been found within the nose and mouth, and limited to these membranes by Fournier.

The vesicles of ophthalmic zoster are usually smaller and more numerous than the vesicles of zoster on other parts of the body. In some cases papules, bullae and pustules may appear instead of vesicles.

The inflammatory period of herpes zoster ophthalmicus is from eight to twelve days, although the ulceration of the skin takes a long

time to heal. In cases of the mild form the lesions leave pigmented spots or scars in five or six weeks, but in cases of severe type many weeks may elapse before the inflammation disappears and healing is complete.

The cutaneous manifestations, in order of appearance, are hyperalgesia, erythema, vesiculation, rupture of vesicles, cicatrization and hyperesthesia.

The extent of the eruption varies a good deal and is almost always confined to one side of the face. Vesicles never extend across the midline except in the case of bilateral herpes zoster, which may or may not be of simultaneous occurrence. This overlapping of the midline has been reported in several cases, but it was probably due to an erythema of the skin with edema, and the eruption was not vesicular in type. Lewis stated that the eruption might extend over the midline because of overlapping of nerve filaments from the opposite side and because the distribution of the fifth nerve is often different on the opposite side. A typical zoster without eruption but with neuralgia may occur.

#### LYMPHATIC GLANDS

The lymphatic glands adjacent to the affected areas are practically always enlarged, and the adenitis may appear at times before the eruption. Ramond and Lebel stated that this adenopathy merits equal rank with the pain and the eruption of the disease, as it renders possible the differentiation of true zoster from a zosteriform eruption. Involvement of the lymph glands is almost always unilateral, is independent of all secondary infection and may be associated with the slightest eruption. The enlarged lymphatic ganglions are those whose afferent lymphatics are derived from the affected zone.

The adenitis is characterized by swelling and pain in one or more definitely movable ganglions and is often unrecognized unless the superficial ganglions are involved. The number of affected ganglions varies. There may be only one, but several are frequently encountered. In cases of herpes zoster ophthalmicus the preauricular gland is enlarged, and sometimes there is subangulomaxillary adenopathy. The submaxillary and subhyoid ganglions are involved in cases of superior or inferior maxillary zoster. The tumefaction may be seen, but most frequently it is recognized only by palpation. The skin over the swelling never shows any change in color unless the gland becomes infected from the vesicles. Pain is elicited by pressure and is not spontaneous, and it is far less severe than the pain of

acute inflammatory adenitis with a tendency to suppuration.

Primary adenitis must be distinguished from secondary, or late, adenitis. The secondary adenitis is due to infection of ulcerated vesicles, with a tendency to suppuration and modification of the adjacent skin, but the mode of production of the primary type is still undetermined. It is possible that it may be caused by the virus of herpes zoster, although most investigators associate it with the cutaneous lesions.

Francois, in 1936, reported 2 cases of herpes zoster ophthalmicus in which preauricular adenopathy preceded all cutaneous eruption by three days. He stated that this observation afforded 2 examples of an atypical zoster and served to confirm the assumption that a primary preeruptive adenitis exists with zoster, and hence elucidated the still obscure pathogenesis of zosterian adenitis, namely, that it is caused directly by the zoster virus, which acts simultaneously but independently both on cutaneous nutrition and on the nutrition of lymphatic ganglions. He stated that it is more than probable that posterior poliomyelitis is the initial lesion and that this process acts on lymphatic ganglions, either indirectly, through lesions of the skin, or directly, simultaneously and independently, on cutaneous nutrition, there to produce incipient tumefaction, degeneration of epidermis cells, and on the nutrition of lymphatic ganglions to occasion the simple congestive hypertrophy of these glands. Cuenod and Nataf, Metz and Achard concurred in this opinion, and each reported cases. Other cases have been noted in the literature by Danlos, Barber and Steffan.

Primary zosterian adenitis exhibits its greatest tumefaction and sensitivity at the outset of the eruption, and occasionally even before eruption, then gradually diminishes in severity and finally disappears about the tenth or the twelfth day. Recovery by spontaneous resolution constitutes the natural and regular termination of this adenopathy. The gland never suppurates, the process never progresses to chronicity, and the prognosis is favorable. However, all adenopathy occurring in the course of the disease is not of zosterian nature, and all herpes accompanied with adenitis is not herpes zoster.

#### EYELIDS

In practically all cases, the eyelids are swollen and attended with redness, edema and some induration. The swelling involves particularly the upper lid, the loose cellular tissue of which is readily distensible. Sometimes the eyes are closed, and some exudate usually appears between



the lids. The hyperesthesia may be so great that it is almost impossible to open the lids, especially during the acute stage. Early in the disease ptosis is often present, which may be due to mechanical edema or paresis of the sympathetic fibers to the levator muscle, with mydriasis and paralysis of accommodation, or sometimes with paralysis of the internal rectus muscle or other third nerve palsy. The pseudoptosis which results from edema of the upper lid protects the cornea, and less opportunity is offered for the development of keratitis. Palpebral zoster frequently pursues a course far more serious than zoster of other parts of the body. Involvement of the lower lid offers a more favorable prognosis than that of the upper lid, since hyperemia, edema and vesicles are less severe. Zoster of the upper lid may be serious, and the older the patient, the more its complications are to be apprehended. Tacké, in 1903, reported a case of zoster in a young male in which the entire upper eyelid was covered with vesicles. These underwent suppuration, with resulting deformity of the lid. Carré reported a similar case. Clarke described a case in which the attack of herpes zoster caused destruction of part of the upper lid, exposing the cornea, with resulting corneal perforation. F. A. Phillips, in 1907, cited a case of zoster in a man of 47 years. The blisters of the lids took seven months to heal, resulting in a cicatricial entropion. Barré, in 1924, described a case of zoster with blepharospasm in a female. The author concluded that the determining cause of the reaction lay in the existence of zoster of the internal nasal branch and that there was a partial zona, which is often difficult to recognize. As a rule, however, these disturbances disappear with the termination of the eruption and in general do not indicate a grave prognosis. However, in some cases the ptosis may remain indefinitely after recovery from the disease.

#### CONJUNCTIVA

When the eruption is at its height, conjunctival injection is usually seen, with increased secretion. The conjunctiva is implicated primarily by vascular injection and tumefaction, as with practically all inflammatory disorders and other forms of irritation of the eye, and the bulbar, as well as the palpebral, portion is involved. Sometimes the conjunctival edema may cover the periphery of the cornea, and semipurulent secretion helps mask the conjunctiva.

Simultaneously with the appearance of the initial eruptive elements, vesicles may form in the conjunctiva, although they are difficult to discern on account of swelling and injection. Sometimes

small pustules may be seen in the conjunctiva, which run the same necrotic course, with scarring, or the vesicles may resemble phlyctenular conjunctivitis, with severe pain, photophobia and lacrimation. Scriven (1869), von Arlt (1871), Lagarde (1874) and Sichel (1871) reported cases in which vesicles appeared on the conjunctiva. Wible, in 1917, described a case with conjunctival vesicles, which was the fourth case he had seen in 20,000 cases of disorders of the eye. Stieren, in 1906, reported a case in which many vesicles were present in the conjunctiva of the upper and lower lids. Pfingst cited a similar case. Kreibitz, in 1938, described a case with bilateral conjunctival vesicles. Buhne-mann, in 1937, described a case in a man aged 65 years. The conjunctiva of the left eye, near the outer limbus, showed a nodule, surrounded with vesicles, which were not painful to the touch. The nasal third of the corneal epithelium was loosened and stained with fluorescein. In this case the symptoms involving the conjunctiva of the bulb dominated the picture. Cases of conjunctival vesicles have been reported by Griffith, Michel, Herve, Blachez, Cousin and Périssou, Terrien, Tikanadze, Kinnicutt, Duméry, Lauber, Wurdemann, Schoeppe, Knowles, Aubaret and Master, Couyba, Armagnac, Strzeminski and others.

Complications involving the appendages of the eye are not particularly serious. Conjunctival lesions are often present, the eye is red, and there is a certain degree of conjunctivitis with moderate edema in nearly all cases. Sometimes the conjunctival injection may precede the formation of the vesicles on the skin and often persists long after the disappearance of keratitis.

#### OCULAR COMPLICATIONS

Ocular complications, if any, may be observed in the various phases of herpes zoster, from the first day of onset to a remote date, even months after the healing of all cutaneous lesions. Early investigators stated the belief that complications were nearly always secondary to cutaneous manifestations and observed that inflammation of the eye occurred most often when the eruption was at its height or in the period of subsidence. The most dangerous complication of herpes zoster ophthalmicus, as well as of zosteriform or of secondary eruptions, is extension of the process to the globe of the eye. This occurs in about 50 per cent of cases, causing disturbances in the transparent media, the iris, the sclera, the cornea or the muscles. Hybord observed such complications in 45 per cent of cases, Hutchinson, in 36 per cent, Pacton, in 68 per cent, Koch, in 55

per cent, Buhemann in 50 per cent, Worster-Drought, in 50 per cent R F Moore, in 60 per cent, Achard, in 60 per cent, Gundersen in 50 per cent, and Rollet, in 75 per cent. Involvement of the cornea is observed in practically one third of all cases of ophthalmic zoster a complication which enhances the gravity and often governs the prognosis of the disease. Spicer (1907) found this complication in 25 per cent of cases, Cantonnet, in 35 per cent, Paton, in 35 per cent, Agnello, in 40 per cent, Cohn, in 25 per cent, Hybord, in 43 per cent, Achard, in 35 per cent, and Wilbrand and Saenger in 35 per cent. I found it in 35 per cent of 2,250 cases.

#### CORNFA

*Corneal Anesthesia*—The corneal eruption is usually preceded by a period of insensitiveness, which renders possible the anticipation of keratitis. Corneal anesthesia should always be looked for, since it invariably entails the possibility of grave ocular complications. The anesthesia may occur simultaneously with the eruption or may appear with the subsidence of the herpes zoster. It is usually transitory, and recovery of corneal sensibility takes place during a period of months or it may take years. In certain instances anesthesia of the cornea, appearing without a lesion of that membrane constitutes the only symptom of corneal zoster. Mere anesthesia of the cornea, with dryness and impaired vasomotor reaction cannot be regarded as the essential factor in production of the keratitis. In testing for corneal sensitivity, most investigators have used the hair apparatus of von Frey. Pfimlin stated that the threshold of sensitivity of the normal cornea showed a value of from 5 to 10 Gm per square millimeter for recognition of contact and of from 10 to 20 Gm per square millimeter for sensation of pain.

*Keratitis*—The cornea is often affected during the course of the zoster and is the seat of the most serious ocular manifestations. Many forms of keratitis present themselves. They may be ulcerative, superficial or deep, nonulcerative superficial or deep or a combination of these forms. In the early stages, there is little, if any infiltration, and the vesicles are easily overlooked as examination is difficult because of the irritation and blepharospasm.

Keratitis the essential lesion, consists of a subepithelial infiltrate composed of round, discrete, opaque dots. These dots are most numerous in the substantia propria but may be seen at lower levels. As a rule the corneal involvement appears at the height of the evolution of the herpes zoster, on the sixth or seventh day.

Cases have been noted in the literature in which the initial lesion was a keratitis. This reversal of form is exceptional, for it is rare that keratitis precedes the cutaneous eruption. Pflüger, in 1874, reported the first case. In Terson's case keratitis developed two weeks before the cutaneous eruption. Similar cases have been reported by Doggart, Veil, Valere-Vialery, and Bussy and Bonamou. Ahlstrom, in 1904, described an unusual case in which corneal zoster was the only form of involvement of the fifth nerve in the course of zoster of the lumbar plexus. Von Hoffmann in 1879, described a similar case but without the cutaneous eruption.

It is customary to consider two forms of keratitis as occurring in the course of herpes zoster ophthalmicus aside from the accidental complications. One form is characterized by the occurrence of groups of minute transparent vesicles, resulting from elevation of the epithelium and situated usually at the nasal periphery. The other form is characterized chiefly by the invasion of the deeper parts of the parenchyma or the interstitial tissue, without vesicular eruption or effect on the epithelium. Some authors claim that superficial lesions are exceptional, and since their appearance is rarely detected, their existence has been questioned by some investigators. J. Rollet in 1932, stated that he had never observed this superficial form. He expressed the belief that there was only one form of keratitis and that interstitial lesions were constant, as in the skin. However, superficial vesicles do occur, and they have been demonstrated in many cases, but deeper infiltrates may appear in the course of the disease, with or without any superficial lesions. Epithelial edema is a constant factor.

Parsons in 1912, stated that most herpetic lesions were superficial, while Paton, in 1926, concluded that the majority of corneal lesions consisted of deeper corneal infiltrations and that the subepithelial infiltrate was the initial lesion. Wangler stated a similar opinion in 1889 and reported 6 illustrative cases.

The corneal vesicles, if present, are usually multiple and may appear in groups and rupture, leaving small shallow areas of ulceration, which tend to coalesce and leave crenated borders. These small ulcers usually heal rapidly and may be followed by fresh crops of vesicles, or the ulcers may enlarge and fuse, leaving a large cloudy area of denuded epithelium. Secondary infection may occur, forming deep central or peripheral ulcers, which may result in perforation. Corneal denudations have a variable result. A simple ulceration may leave a leukoma, while

other ulcerations may leave numerous nebulas. Some opacities always remain, and pannus may develop. In some cases the vesicles may be accompanied with deep corneal infiltrates without ulceration, while in others the corneal vesicles develop without perceptible corneal infiltration. Irregular, gray opacities are noted at various depths, with haziness and edema, which may or may not be preceded by vesicular eruption. The corneal infiltration may precede the vesicular eruption in the cornea and in the skin and may heal with it, leaving as a sequela a more or less dense zone of anesthesia.

Descemet's membrane may show folding. Paton asserted that this was due to hypotonia, while Doggart claimed that it was the result of keratitis. Rollet stated that either the deep striae in the cornea were due to the folds in Descemet's membrane or they represented dehiscences between deeper layers of the stroma. Cloudiness of the cornea was noted in connection with these folds. Precipitates on Descemet's membrane have appeared frequently but are often difficult to see without the slit lamp. Rollet reported a case in which the cornea was involved, and examination with the slit lamp showed numerous striae at different levels of the cornea, with considerable precipitation on Descemet's membrane. The iris was normal, and there were no synechias.

Deep corneal infiltrates may appear, which may or may not leave a permanent scar, and deep infiltrates may form which do not undergo purulent disintegration. Often ulceration occurs, which may be compared to that of neuroparalytic keratitis following section of the trigeminal nerve, that is, it develops slowly, without any tendency toward spontaneous cicatrization, extends gradually, is accompanied frequently with interstitial infiltration and later may leave a dense leukoma. Paresis of nerves may remain, and neuroparalytic keratitis may occur. Cases of this complication have been reported by Cross, Ginsberg, Jacquieu, Gillette, Kroll and Hybord. In the cases reported by Lafon and Villemonte the neuroparalytic keratitis developed six weeks after the onset of the herpes zoster. However, neuroparalytic keratitis does not necessarily always occur with paralysis of the sensory root. Clinical results suggest that it is a symptom of irritation and not the result of paralysis of the sensory division. The nutritional state of the fibers of the fifth nerve depends on the cells of the gasserian ganglion. Fibers beyond the ganglion degenerate if separated from the ganglion by disease. This degeneration usually means keratitis and loss of the eye, and the keratitis occurs

during the active process of degeneration of the nerve fibers. Redslob expressed the belief that corneal opacities observed during herpes zoster not only represent disturbances of neuroparalytic character but constitute the true eruptive foci.

Deep corneal infiltrates may form which are similar in clinical appearance and course to disciform keratitis. Cases have been reported by Cross, Neame, Wangler, Sulzer, Wilbrand and Saenger, and Schenkl.

Parenchymatous keratitis may occur at the onset of herpes zoster ophthalmicus as a complication, or it may appear frequently as an end result of corneal vesicles. The vesicles on rupturing induce a superficial ulceration, which, in turn, may produce keratitis. The infiltration is not due to corneal ulceration, and the epithelium of the cornea remains intact. The majority of authors describe parenchymatous keratitis as a rare complication. It is assumed that this keratitis results from an epithelial erosion which the corneal vesicles leave after rupture, and keratitis without epithelial lesions is said to be exceptional. However, Valière-Vialeix opposed this view. In a study of 17 cases, he observed interstitial keratitis in 13, in 5 of which epithelial lesions were present, but he concluded that the superficial lesions were secondary, or at least that the superficial and the deep lesions appeared simultaneously. He stated that parenchymatous keratitis is the form customarily and most frequently associated with herpes zoster ophthalmicus and that, in any event, lesions of parenchymatous keratitis do not represent the end result of superficial lesions, in consequence of a gradual extension. He concluded that the two forms of keratitis were independent lesions, two different localizations of the zoster infection, and that they have an independent evolution, namely, corneal vesicles and parenchymatous keratitis. Satanowsky, in 1931, reported 2 cases in which there was no superficial involvement of the cornea. Similar cases have been described by Koster, Ahlstrom, Leopold, Moret, Rollet and Grand-Clement, Schiess-Gemuseus, Ginsberg, Tsiekhanovich and Márquez.

Holzer reported an unusual case of corneal opacity following herpes zoster ophthalmicus. One year after an attack an irregular circular opacity developed near the nasal limbus. The epithelium was intact, and corneal sensitivity was diminished. No cause could be found for the unusual opacity. The results of all laboratory tests were noncontributory, and physical examination revealed no abnormality. Gradually the opacity became less dense. Examinations with the slit lamp made at intervals disclosed at first a milky



appearance, with an irregular epithelial surface and many white deposits below. As the opacity extended, there appeared at the margins a dense line of yellow deposits. These deposits disappeared one month later. Folds in Descemet's membrane were observed, which later also disappeared. Lister reported a similar case of dense spreading corneal opacity following herpes zoster. One year later the ulcer was 2 mm in diameter, with smooth epithelium and good corneal lustre. At no time was there any inflammation of the cornea.

Hypopyon and sloughing of the cornea have been reported in many cases by Jeffries, Lacausade, Calhoun, Noyes, Sommer, von Hoffmann, Spicer, Smith, J. Hutchinson, Da Fonseca, Elliot, Dumery, Teulon, Galezowski, Eyer, Adler, Lucic, Randolph, Hirschberg and others. In many of these cases, and in others the corneal lesion has resulted in perforation and enucleation has been necessary. In the case of hypopyon reported by Klauber, in 1918, there was no corneal infiltration, but iritis was present. Meller expressed the belief that disease of the trigeminal produced tissue defects within the iris, which led secondarily to necrotic foci, these, in turn, caused purulent inflammation.

Relapse of the corneal infection is common, for the damaged epithelium is unable to resist exposure and the vitality of the cornea is lowered. Serious ocular conditions may follow. A co-existent iridocyclitis and descemetitis may add to the decrease of corneal resistance. These lesions interfere with vision, ordinarily persist for several weeks and are a great source of annoyance to the patient. Diminution of vision due to paralysis of accommodation should be carefully differentiated from that which involves degeneration of corneal epithelium. Confusion is possible because this superficial ulceration of the cornea may at the onset be visible only with indirect illumination or after the use of fluorescein.

Localization of interstitial alteration of the cornea in a circular zone or in one section of the cornea constitutes a characteristic of herpes zoster ophthalmicus. Bonnet, in 1939, reported the occurrence of such localization in a male patient, on the third day after the cutaneous eruption. Anesthesia of the cornea was noted near 2 o'clock, localized in the superointernal sector, the rest of the cornea, on the contrary, was hyperesthetic. Later, interstitial disturbance manifested itself in the area of anesthesia, subsequently minute vesicles appeared in this area and finally ulcerated. Descemetitis soon developed. Bonnet and Colrat noted the frequency of this limitation of the disease to one sector and

stated that this topographic pattern in interstitial alteration of the cornea was governed by the exclusive involvement of one nerve fiber of the cornea, namely, the fiber corresponding to the meridian affected. Guillain, Lagrange and Perisson, in 1926, reported a case in which the cornea was involved. Examination of the corneal reflex demonstrated that sensibility was intact in the central part of the cornea, the sensory innervation of which pertained to the ciliary nerves. On the contrary, the conjunctiva and the periphery of the cornea, to which were distributed the terminal branches of the ophthalmic nerve, were anesthetic, but no difference could be noted between zones innervated by these various nerve branches. Molter described the case of a female with opacity of the entire half of the cornea. Tests for sensibility revealed complete anesthesia in the region of the denser opacity of the cornea, with diminished faculty of sensation for contact and pain in other opaque areas, and diminished pressure sense and complete abolition of temperature sense in the areas of most marked opacity. It is conceived that certain ciliary nerves may be affected exclusively and that this limited involvement may present itself as an alteration in one sector of the cornea.

#### MODIFICATION IN OCULAR TENSION

Increased ocular tension may be classified as two types: the first comprising accidental occurrences of hypertension associated with iridocyclitis of zosterian origin, and the second involving acute or chronic glaucoma without iritis. It is questionable whether the latter type is due to zoster as a specific etiologic agent or whether, rather, it is due to a condition such as pneumonia or bronchitis, for these diseases are capable of precipitating glaucoma in a properly predisposed eye. The glaucoma is generally of acute unilateral type, on the same side as the eruption, and is characterized by dilatation of the pupil, pericorneal injection and severe pain. The increase in tension usually appears within fifteen or twenty days after the eruption, but rarely precedes it.

In the first form the rise in tension is probably due to involvement of the iris and the ciliary body, whether or not the cornea is affected. In an eye predisposed to glaucoma, herpes zoster is capable of precipitating an attack. Morav (1916) held that herpes zoster awakens a latent glaucomatous condition. This was seen in a case of glaucoma precipitated in the course of zoster of the first branch of the fifth nerve, without involvement of any structure of the eye, as reported by Dubois, in 1912. Weeks stated

that glaucoma following herpes zoster ophthalmicus was no doubt due to changes in the composition of the aqueous, which render it less diffusible and prevent proper filtration through the lymph channels at the angle, as lymph spaces do not easily tolerate foreign products. In many such cases of glaucoma following iridocyclitis atropine has been of benefit. Morax (1916) cited 2 cases of glaucoma secondary to iridocyclitis. Other cases have been reported by Knapp, de Schweinitz, Hirschberg, Clark, Parker, Woods, Lodge and Lodge, Elliot, Dubois, Erdmann, Rea, Weeks, Veasey and Königstein and others.

Sometimes the tension is high early in the disease, and later it is lowered. It is often lowered while the inflammation is subsiding. It is usually low when folds are seen in Descemet's membrane or when atrophy of the ciliary processes is present. When the ocular tension is determined throughout all periods of the disease, there are seen many variations which are transitory and invariably fluctuate widely about the normal tension. Cases in which the tension is decreased have been reported by Horner, Maillet-Guy, Goldzieher, Horstmann, Achtermann and others. Sedan stated that hypotension occurs not only in connection with corneal lesions but with conjunctival lesions and is most marked with ulceration and vascularization of the cornea. He stated that hypotension was never encountered in the presence of an intact cornea. Rollet expressed the same view. Sasportas, in 1913, reported the case of a man aged 59 years. One week after the initial appearance of the herpes a large hemorrhage developed in the anterior chamber. The cornea was anesthetic. The iris was moderately dilated and failed to react to light, and at certain points it presented ecchymoses. The tension was elevated. Later the volume of the globe appeared to diminish and presented evidence of incipient phthisis. After a time the tension became elevated, and the globe recovered its normal volume.

In many cases the disease has been ushered in with acute glaucoma. Such cases have been cited by Bradburne, Kennon, Bane, Scott, Lewis, Hartz, Rollet, Bussy and Bonamour, Jacquet and Pantol. Brav reported such a case and expressed the belief that the increase of tension was due to zoster of the fifth nerve, as this nerve is a vasodilator and may cause not only hyperemia but stasis which may give rise to acute glaucoma. Pierson stated the belief that hyperemia of the vessels accounted for the secondary glaucoma. Urrets Zavalia asserted that ocular hypertension is an initial symptom of herpes zoster ophthalmicus and recorded 2 cases. The glaucoma in

these cases preceded the eruption by several days. There was no involvement of the cornea or iridocyclitis in either case. Colrat, in 1931, described another case in which the disease was ushered in with acute glaucoma.

Modifications of ocular tension are secondary. When hypertension develops in cases of interstitial keratitis, the tonus may increase until glaucoma is noted. On the other hand, when the tension is decreased, there is usually present an iritis, which changes the regulatory system of the eye, precipitating hypotonia, or even in some cases phthisis bulbi may develop. Symptoms resulting from these disturbances of tension may also be seen when inflammatory complications are not present or have disappeared. In such circumstances a direct action of the sympathetic nervous system is assumed.

#### IRIS

Next to the cornea, the anterior uveal tract is most frequently affected with herpes zoster. In most cases in which the cornea is involved some iritis is present, with contracted pupil and photophobia. In other instances a true iridic inflammation may develop, with intense pain, redness, miosis, disturbed vision and posterior synechias, leading sometimes to hypertension. Every case is characterized by a small pupil, the result of irritative reflex miosis, unless there has been a paralytic mydriasis, due to irritation of the ophthalmic ganglion, or posterior synechias, due to the presence of plastic exudate. In some cases degeneration of the iris results, followed by atrophy of the ciliary processes and phthisis bulbi. Heterochromia may gradually develop at times. Cases of this type have been reported by Genet, Federici, Igersheimer, Viallefont and others.

The iritis may not appear until late in the course of the disease. Cases of this type have been cited in the literature by Paton, Kosminski, Horstmann, Michel, Wyss and others. Or the iritis may appear at the same time as the keratitis, as reported by Sattler, Noyes, Koch and Cohn. Or it may occur when the corneal complications are subsiding, as described by Crisp, Rollet, Ishiwaru, Huguet, Pacton, Chance, Martini and Sattler. In some cases the iritis may appear before the cutaneous eruption, as reported by Bussy and Bonamour, Gould, Johnen and Jorissenne. Iritis without preceding keratitis is exceedingly rare, but cases of this kind have been noted in the literature by Paton, Bowman, Satanowsky and Jelkovich, Lafon and Villemonthe, Machek, and Meller. Primary iritis, if undetected, may produce grave posterior syne-

chias This form, Rollet stated, is latent and might be compared in its insidious course with precocious secondary syphilitic iritis Gilbert, in 1921, mentioned 9 cases of primary iritis that he had encountered and reported 2 of his own In his first case a man aged 49 was seen ten days after he first complained of severe pain in his forehead Some conjunctival hyperemia was noted, the iris was steamy, and corneal anesthesia was present Hypopyon developed, and blood was noted in it During the next few months thirty-five small hemorrhages occurred in the anterior chamber The tension gradually increased Five years later the eye was enucleated Gilbert stated the belief that the iris was often affected in this disease, not as a result of secondary spreading of the corneal process to the iris but as a genuine primary herpetic disease of the uveal tract, characterized by initial neuralgic pain and circumscribed swelling of the iris, with hyperemia and often with hemorrhage

It is difficult to determine whether iritic hemorrhage is possible without previous inflammatory reaction, although Sasportas, in 1914, reported a case in which hemorrhage from the iris into the anterior chamber occurred without previous inflammation of the iris Machek, in 1895, described in great detail a case in which hemorrhagic iritis developed As a result of continual pain and a disturbed nutritional state, the man died two years later The cornea was not involved Tension was reduced The pathologic changes in the iris began with neuralgic pains in the eye, followed by hyperemia and inflammation of the iris, with plastic exudate and resulting adhesions

Swelling of the pupillary part of the iris with hemorrhage into the anterior chamber was termed herpes zoster of the iris by Machek, Gilbert, Verhoeff, Zeeman, Schoeppe and Lowenstein Rollet stated that actual zoster iritis often pursued a chronic course If it was acute, the patient usually became extremely ill, in consequence of the intense pain and headache, and was often unaware of the disease of the eye In addition to this genuine type of zoster iridis, Rollet defined profound iridokeratitis, with or without increase of tension, in which the anterior corneal epithelium is completely intact and the opacity is interstitial

Meller asserted that the focal areas of hyperemia with the iris were not due to vasodilator phenomena directly but, rather, resulted from inflammatory reactions brought on by destruction of tissue The theory of trophic disturbance must be abandoned, as removal of the gasserian

ganglion frequently has not led to disease of the iris

#### SCLERA

Scleritis is a rare complication of herpes zoster ophthalmicus and usually occurs late, in association with keratitis or iridocyclitis The scleral nodules are small, circumscribed, red, painful areas with translucent centers The conjunctiva over them is smooth and congested and may be adherent After many weeks, or sometimes months, the nodules become smaller, without ulceration, and leave a slate blue discoloration of the sclera The iris often becomes atrophic nearest the nodules in the sclera The pupil may be inactive or may be dilated Relapses are common, and fresh nodules arise in areas of the sclera hitherto unaffected Cases have been reported by Kendall, Lauber, Mayou, Stellwag von Carion, Thompson, Meller, von Hoffmann, Penman, Jeffries, Clavelier, Strzeminski, Sourdille and Legrand, Fassbender, Doggart and Goldberg Genet reported several cases, and in 1 of them a similar eruption appeared in the other eye four years later Verderame, in 1913, described a typical case of this complication in a woman of 54 years The left frontal region, the left side of the nose and the region of the external commissure of the left eye showed extensive involvement of the skin The preauricular glands on the left side were congested The globe was injected, with punctate keratitis Six weeks later perikeratitic injection was pronounced The sclera exhibited two elevations, of a reddish violet color, which were painful on digital pressure At this time ocular tension increased and posterior synechias were present Six months later the orbital pains had disappeared The sclera exhibited two areas, of a slate red color, which at this time were painless on pressure, and ocular tension was reduced to normal Terrien, in 1900, reported an interesting case of a woman of 59 years, in which there was first noticed in the superoexternal part of the scleral region a red, infiltrated, painful area of episcleritis This soon spread to the cornea and presented a diffuse infiltration, which extended to the pupillary area The corneal epithelium remained intact The pupil was contracted and reacted faintly to light About ten days after the ocular involvement an eruption of vesicles appeared over the left frontal region, preceded for two days by intense pain over the entire left side of the head This case, again, emphasizes the occurrence of primary ocular manifestations, as an initial symptom of herpes zoster, several days before the cutaneous eruption

## INVOLVEMENT OF THE NASAL NERVE

Ocular complications of herpes zoster are particularly frequent when the eruption invades the territory of the nasal nerve. The form which is generally confined to the anterior segment of the eye is most often characterized by an eruption of vesicles on the anterior surface of the cornea. Bowman, in 1869, and Hutchinson, in 1869, stated the opinion that the cornea is never involved unless the nasociliary nerve is affected, but Vernon, Coppez and Cohn found exceptions to this rule and noted, also, that when the nasociliary branch was affected the cornea was not always involved, as in cases reported by Douglas, Jeffries, Moers and Wadsworth. Hybord modified the rule expressed by Bowman and Hutchinson by stating that the cornea and iris are rarely affected unless the dermal eruption occurs in the region supplied by the nasociliary nerve, but that they are usually involved if the entire side of the nose, or the ala nasi alone, is covered with vesicles. Hybord in 1872, reported 53 cases in which the tip of the nose was involved, in 35 of which ocular lesions were present. Ahlstrom, in 1904, submitted 50 cases. The cornea was affected in 23 and the nasociliary nerve in 20 cases. In 3 cases the cornea was involved, but the nasociliary nerve was not disturbed. Teulières and associates, in 1933, asserted that invasion of the internal nasal nerve is always accompanied with lesions of the cornea.

The worst ocular complications of herpes zoster ophthalmicus are generally associated with vesicles along the nasal nerve. While it is generally assumed that involvement of the nasal branch entails the hazard of ocular complications, numerous observations have shown that iritis and corneal scars may occur when the nose is free from eruption and, conversely, that these ocular complications may fail to appear when zoster has attacked the root of the nose and the side of the nose all the way to the tip. Instances in which eruption covers the entire side of the nose without affecting the eye are explained by involvement of the ramifications of the second branch of the nerve. Wadsworth attributed the distribution in a case in which the tip of the nose was affected but the cornea remained clear to an anatomic anomaly, described by Turner, in which a small supratrochlear branch of the frontal nerve joins the infratrochlear branch of the nasociliary nerve. In such a case the herpes zoster confined to the frontal nerve includes the nose but not the eye. Disease of the globe, with absence of eruption on the nose, is attributed to alteration of the single ocular portion of the

oculonasal nerve, whose course is endonasal but becomes external only in the inferior portion of the nose. As a general rule, the eye scarcely ever suffers much when the nose is not affected, and the severity of the eruption on the nose is usually in direct relation to the severity of the ocular symptoms. But it does not follow that the eye is exempt when only the forehead exhibits eruption of vesicles. Rollet observed ocular lesions with zoster frontalis as well as with zoster lacrimotemporalis.

In many cases the lacrimal nerve is involved, and vesicles may appear on the skin of the lids, the conjunctiva and the side of the nose. It is often difficult to tell whether or not the lacrimal nerve is affected unless there is a great deal of eruption on the upper lid, with edema and injection of the conjunctiva. The fibers of this nerve run alongside the frontal nerve.

## DISTURBANCES OF THE SYMPATHETIC NERVE SUPPLY

In cases of ophthalmic zoster disturbances of the sympathetic nerves may assume the form of the Claude Bernard-Horner syndrome, and the complex has been reported in some cases, with enophthalmos, contraction of the palpebral fissure and miosis. Typical cases were described by Aubaret and Morenon, in 1927. In 1937 Federici reported a similar case. He stated the belief that in this case the virus of herpes zoster ascended the nasal branch of the ophthalmic nerve and was transmitted by a fine branch of the sympathetic nerve, producing the syndrome. Jacquet and Bariéty, in 1926, reported the case of a woman of 32 years with corneal anesthesia, enophthalmos and diminution in size of the palpebral fissure but no miosis. Miosis rapidly developed after administration of physostigmine and persisted a long time. On the contrary, atropine induced only slow and gradual dilation of the pupil. The difference in the effect of atropine and physostigmine on the affected eye and that on the other eye was evident. This complex continued to exist for approximately three weeks after healing of the cutaneous lesions. Jacquet and Bariéty concluded that the condition was due to paralysis of the sympathetic fibers. Talkovskiy, Rollet and Colrat, and Spicer (1907) described cases in which dysfunction of the sympathetic nerve supply was the cause. Ligertwood, in 1927, reported a case in which there was a lesion of the sympathetic nerve, which paralyzed the dilator pupillae, and a lesion of the oculomotor nerve, which paralyzed the sphincter. The author concluded that the sym-

pathetic nerve supply was injured in an operation on the glands of the neck, previous to the present illness, and that the oculomotor nerve was involved as a result of the herpes, causing mydriasis and paralysis of accommodation. Potts reported a case of paralysis of the pupillary sympathetic fibers and the ophthalmic division of the fifth nerve following an attack of herpes zoster ophthalmicus. The pupil was contracted and did not dilate when shaded or when cocaine was instilled but contracted when stimulated with light. Rosnoblet reported 2 cases of the syndrome in consequence of spasm or paralysis of the sympathetic fibers. Leriche and Fontaine stated the belief that in man some sympathetic fibers with ocular destination leave the first thoracic ganglion to follow the vessels and that ptosis after section of the sympathetic trunk is an active phenomenon, as it can be exaggerated by irritation of the sympathetic chain or can be made to disappear by removal of a neuroma. Some of the musculo-orbital fibers must leave the cervical sympathetic chain below the superior cervical ganglion, as excitation of a neuron of this chain increases the ptosis after suppression of the upper cervical ganglion. Aubaret and Margailan, in 1923, reported a case of the syndrome in a man of 70, with miosis and contraction of the palpebral fissure, which they attributed to involvement of the sympathetic fibers. They expressed the belief that the filtrable virus became lodged in the sympathetic ganglions, either orbital or of the cervical chain, and produced the concomitant syndrome of miosis and contraction of the palpebral fissure. Starobypinska and Sterling, Dufour and Urrets Zavalía cited similar cases. Anatomic investigations conducted on the spinal cord of patients with herpes zoster have revealed lesions of the anterior horns of the cord and lesions involving radicular ganglions and fibers of the posterior funiculi. As the sympathetic nerves have a close relation to the spinal cord, it is conceivable that they may be affected to some degree in the form of paresis of the sympathetic fibers.

#### ARGYLL ROBERTSON PUPIL

Pupillary disturbances of purely nervous origin, without resultant iritis, may occur in conjunction with herpes zoster ophthalmicus, and the Argyll Robertson pupil has been noted in several cases. The sign appears late, often months after the eruption, is unilateral and is seen on the side on which the zoster had appeared. Verhoeff, in 1919, described a case of the syndrome which he believed due to a lesion

in the ciliary ganglion. Redslob, in 1923, reported a case in a woman aged 66. The left pupil was dilated and did not react to direct or indirect illumination but did react in convergence. He stated that this observation proved that convergence exerts a more powerful action than luminous excitation on contraction of the pupil. Lesions of the ciliary ganglion nullified the effect of photomotor excitation on the sphincter but were insufficient to prevent the more energetic action of convergence.

Genet, in 1925, reported a case of a woman of 56 years. The pupil of the left eye was in a state of moderate dilatation, with complete immobility to light. The pupillary paralysis followed the disease of the skin and was present one year later. He stated the opinion that it was due to a lesion of the ophthalmic ganglion, consequent on primary irritation of the ophthalmic nerve by way of the nasal root of this ganglion. Although it is impossible to exclude deeper causes of pupillary disturbances, either in the nuclei of the oculomotor nerve or at the base of the encephalon, since zoster itself may be a manifestation of lesions which reveal themselves later, Magitot concluded that the ciliary ganglion is the true motor center which controls constriction of the pupil and stated that any alteration of this ganglion during herpes zoster probably accounted for the pupillary disturbances. Aurand asserted that the pupillary irregularities were toxic in origin. Valiere-Vialeix reported a case in 1931 and stated that only 2 cases of unilateral Argyll Robertson pupil following herpes zoster ophthalmicus had been reported. Cousin and Perisson described a case of a woman of 64 years. There was no corneal lesion, but conjunctival vesicles were present. The pupil did not react to light, although the reflex on convergence remained normal. Nothing in the examination of the patient warranted a suspicion of syphilis. The tests on the blood and the spinal fluid gave negative reactions for syphilis, and no clinical or biologic stigmas were present. Guillain, Lagrange and Périson, in 1926, described in detail a case of the Argyll Robertson sign in a man of 51 years. The intrinsic motility was intact in each eye so far as it related to accommodation. However, on the right side, there was encountered complete pupillary inertia to luminous excitation, in contrast to conservation of movements associated with accommodation and convergence and of movements associated with opening of the eyelids. The Argyll Robertson sign, which was of recent appearance, could not be considered



syphilitic in nature. There was no history or stigma of this disease, and tests on the blood gave negative results. In repose there was no anisocoria. Under the influence of light stimuli the left pupil alone contracted. Convergence was accomplished by pupillary contraction, which was equal on the two sides, this response is not obtained in cases of anisocoria. There were no paralytic disturbances in the territory of the oculomotor nerve. The nonparalytic character of the motor disturbance of the right pupil was confirmed by the fact that there was no mydriasis or disturbance of the function of accommodation. Moreover, conservation of the synkinetic movement (enlargement of the pupillary orifices at the moment of opening of the lids) would argue against the existence of iridoplegia, for if there is paralysis of the iris this phenomenon is not present. Guillain and associates concluded that the pupillary phenomenon was due to a lesion of the ciliary nerve and of the ganglionic cells thereto attached. This served to confirm the existence of peripheral motor centers of the pupil, a local ganglionic center disseminated in the parenchyma of the iris, as in the choroid or in the ophthalmic ganglion. Ciotola, in 1936, reported the observation of this type of pupil in conjunction with herpes zoster ophthalmicus in a woman of 36 years. The right pupil was narrower than the left, it was vertical, with absence of photomotor reflex, although reaction to accommodation and convergence were present. Gradual and insufficient dilation of the pupil followed the instillation of atropine. He assumed the existence of an encephalitic focus between the pupillomotor path and the oculomotor nucleus. Satanowsky, in 1931, reported 2 cases of this pupil with no synechias. He stated the belief that the sign is due to an inflammatory process, which may impair the function of muscle cells, innervated either by the sympathetic or by the common oculomotor nerve and leaves more or less extensive areas of atrophy. He discussed the reason for the failure of the pupil to react to light when the nerve is intact and the muscle retains its contractile function. He concluded that in pupillary disturbances of herpes zoster ophthalmicus there is only a manifest disease in muscular function and that an intense stimulus may produce contraction and that since the accommodative stimulus is greater than the luminous, the impression of the Argyll Robertson pupil is created. Localization of the process in neurons intercalated between the nucleus of the common oculomotor nerve and the anterior quadrigeminal bodies is not in accord with his

observations, in which pupillary reaction in convergence and accommodation is not entirely preserved. Moreover, existence of a partial reaction of the pupillary margin to light, which in one observation appeared a year and a half after the eruption, argues against localization of the lesion in the opticopupillary reflex arc, as in cases of tabes and progressive dementia paralytica. In explanation of the fact that the Argyll Robertson pupil does not always appear after severe iritis which has left numerous synechias, it is pointed out that this form of iritis is superficial, while the iritis of herpes zoster is deep and leaves no synechias. Milian and Chapiroau, Wolff, Hermann, Genet, Herman and Zutt have described similar cases.

It is reasonable to assume that there is involvement of the muscles of the iris, due to lesions of the ciliary nerves and of ganglion cells attached to them. This is the result of implication of the ophthalmic ganglion or of local centers disseminated in the parenchyma of the iris. Redslob concluded that alterations of the pupil were due to inflammation of pupillary fibers in the ciliary ganglion and explained the disappearance of the pupillary reflex to light and the persistence of the reflex in convergence by the fact that fibers which conduct impulses of light were destroyed first. According to Redslob, it is reasonable to suppose that fibers which conduct afferent impulses for convergence would themselves be sooner or later altered. Redslob stated the opinion that this type of pupil following herpes zoster was transitory. Meller expressed the belief that ciliary perineuritis is pathognomonic of herpes zoster, since it is not present with such trophic disturbances as neuroparalytic keratitis, which produces high lesions of the trigeminus. Anatomic study of eyes affected with herpes zoster, acute iritis and the Argyll Robertson pupil is necessary to determine the relation between inflammation and infiltration of muscles of the iris.

#### SYMPATHETIC OPHTHALMIA

Occasionally, cyclitis is associated with iritis and may cause blindness and atrophy of the diseased eye and threaten the sound eye with sympathetic ophthalmia. Cases in which this complication occurred have been reported by J. Coppez, Noyes, Jeffries, Guerin and Sommer.

#### EXOPHTHALMOS

There occurs sometimes in cases of herpes zoster a transitory exophthalmos, with or without hypertension, a complication which accords

closely with the theory of sympathetic excitation. Exophthalmos, as a complication, has been reported by ten Doesschate, Vazquez Barriere and Voisin. They stated that the proptosis was due to stimulation of the sympathetic fibers. In the case reported by Vialeix, Prosper-Veil and Isnel the proptosis was believed to be due to inflammation of retrobulbar tissue. Carmody and Batignani described similar cases, and each stated a similar opinion. Viallefont reported a case of herpes zoster with cutaneous lesions of the upper lid, occasioning the formation of scabs, which prevented the closure of the lids, so that lagophthalmos was superimposed on corneal anesthesia. Blepharorrhaphy was performed, with excellent results. This association of corneal ulcer due to corneal anesthesia with mechanical lagophthalmos was regarded as noteworthy.

#### ZOSTER OF FACIAL NERVE

Trigemellofacial zoster is the involvement of the fifth and seventh nerves in the course of the disease. Approximately 110 cases have been reported in the literature, by Fuchs, Chance, Hunt, Vogel, Vargha, Eichorst, Murphy, Ironside, Montgomery, Murzin, Barré, Weill and Reys, and others. Most authors feel that a double lesion of two adjacent ganglions is involved, the gasserian and the geniculate. The clinical picture is that of facial paralysis, with vesicles on the ear and vesicles along the ramifications of one or several branches of the fifth nerve. All three branches of the nerve were involved in the case reported by Baldenweck and Degorce, in 1939.

The anatomic relations between the fifth and the seventh nerve render possible the understanding of some obscure types of ophthalmic zoster. The facial nerve is represented almost entirely by its motor root. Its sensory root is formed by the intermediary nerve of Wrisberg, which, by way of its intrapetrous course, enters the geniculate ganglion. Some sensory fibers extend beyond the last peripheral segment of the aqueduct and become involved with motor fibers of the trunk of the facial nerve. From that small collection of sensory fibers is developed the chorda tympani, which with the lingual nerve, a branch of the trigeminus, shares in sensory innervation of the anterior part of the tongue.

Powell reported a case in which paralysis of the right side of the face developed, with loss of taste on the right side of the tongue and a continuous tingling sensation on the right side

of the tongue and throat, as low as the thyroid cartilage, indicating involvement of the fifth, seventh, ninth and tenth cranial nerves. The voice was weak and hoarse, and the right uveal cord was less responsive in phonation. There was partial anesthesia of the right side of the palate and pharynx. The facial paralysis improved at once after extraction of two dead molar teeth, and the voice and the tingling sensation in the throat and tongue immediately improved. Claude and Schaeffer, in 1912, described a similar case. Klippel and Aynaud, in 1889, collected 17 cases of facial paralysis with herpes zoster ophthalmicus. According to their observations, facial paralysis usually appears during the first days of eruption. It is unilateral and is situated on the same side as the zoster, and there is rarely any paralysis of muscles other than those of the face. However, cases in which ocular muscles were involved have been reported by Barrière, Letulle, Raynard, Heydemann, Caspar and others. Caspar and Murphy each reported a case in which the facial nerve was affected on the opposite side. Paralytic complications of the third and seventh nerves imply extension of lesions to these cranial nerves, and the numerous anastomoses of filaments of the fifth nerve with other cranial nerves would explain these involvements of other nerves. Letulle, in 1882, reported a case of facial paralysis in a male. On the twentieth day of illness partial paralysis of the right facial nerve developed, affecting the superficial muscles but leaving the tongue and palate intact. Strubing, discussing this case, stated the belief that the facial paralysis was 'due to peripheral neuritis of the first branch of the fifth nerve and that peripherally the infective process spread to the fine anastomoses of the facial nerve. From here the disease process extended centripetally in the fibers of the facial nerve until the paralysis developed.

Association of facial paralysis with herpes zoster ophthalmicus is a relatively infrequent occurrence. Rollet remarked the rarity of its development. Voight contributed 1 case and assumed that a neuritis common to the fifth and the seventh nerve was the origin of the condition. Eulenberg stated the belief that zoster was essentially a lesion of the facial nerve and that the seventh nerve conducts fibers the particular excitation of which provoked the zoster. Ebstein asserted that there was no relation between the gravity of involvement of the fifth and that of the seventh nerve and no chronologic relation in disturbance of the different nerves and concluded that there could be no relation of cause

and effect in the involvement between these two nerves. Souqueux concurred in this opinion and reported a case in which the cause of the paralysis of the seventh nerve had to be sought in zoster of the ear, which in his opinion is an indispensable factor in zosterian paralysis of the seventh nerve. In the case described by Verneuil the herpes zoster was preceded by facial paralysis by several weeks.

Facial paralysis is occasionally total, but more often it is partial. It is fairly frequent and almost always follows the eruption, if it occurs. Recovery is the rule.

### PARALYSES OF OCULAR MUSCLES

Paralyses of ocular muscles are not exceptional in cases of herpes zoster and are not dependent on the severity of the pain or the gravity of the disease. The paralyses appear with greater frequency the closer to the cephalic extremity the zoster occurs, and they are encountered most often with cephalic zoster, especially with herpes zoster ophthalmicus.

Such paralyses which develop in the course of the disease are commonly observed when the infection involves the ophthalmic nerve. Inasmuch as herpes zoster has a higher incidence in elderly people, complicating oculomotor paralyses have a higher incidence in this group also. The motor complications usually disappear after a few weeks or months, but may persist for a long time after the cutaneous symptoms have disappeared. Zentmayer described a case in which the paralysis was present one and one-half years after the attack. The ocular paralysis usually appears later than the cutaneous eruption, occurring in the phase of scar formation. The paralysis may appear at the same time as the cutaneous eruption, as in cases reported by Gillet de Grandmont and Oliver. Desirat stated the belief that paralytic phenomena of the muscles never appeared before the cutaneous eruption, but Mittendorf, Saint-Martin, Letulle and Schiffer recorded cases in which the paralysis preceded the eruption. Sometimes the paralysis involves several nerves simultaneously, each of which may be individually implicated, either partially or totally. The question has sometimes been raised whether these paralyses are actually complications or whether they are merely concurrent disorders. Most investigators think they are complications because they appear in much the same manner in a large series of cases. Hunt, in a series of 158 cases, found ocular paralyses in 24, or 14 per cent. Worster-Drought, Désirat, and Lloyd and Elliott each observed ocular paralysis in 7 per cent of cases. Hybord found

5 cases of paralysis of the ocular muscles in 100 cases of ophthalmic herpes zoster.

Paralyses of ocular muscles occur presumably from extension of inflammation of the fifth nerve to the motor nerves as they traverse the cavernous sinus and the superior orbital fissure. Some authors have stated that the paralysis is due to an associated meningitis or to extension of the infectious process to the neuraxis, with production of a nuclear lesion, or to involvement of the motor nerves in the anterior horns of the cord, with resultant paresis of the muscles affected. Wyss, in 1871, observed hemorrhages in the muscles and concluded that the muscular paralysis was due to thrombophlebitis.

### THIRD CRANIAL NERVE

The most common complication of the ocular muscles is total or partial paralysis of the muscles supplied by the third cranial nerve, with or without participation of the pupil. I found 96 cases of paralysis of the third nerve in the literature. Rosnoblet stated that these paralyses occurred most frequently from five to seven days after the appearance of the vesicles but that they might appear weeks, or even months, after the eruption. Mittendorf observed a case of oculomotor paralysis that preceded the eruption. Schiffer described another such case. Metz, in 1913, collected from the literature 50 cases of herpes zoster ophthalmicus complicated by involvement of ocular muscles. The third cranial nerve was affected in 32 cases. The paralysis was either total or partial, and the branches supplying the internal or the external ocular muscles or combinations of these branches were affected. About 25 per cent of paralyses of the third nerve were complete. Many cases of paralysis of this nerve have been described in the literature by Hunt, Valière-Vialeix, Essen-Möller, Ardouin, Silcock, Wallace, Brissaud, Burwell, Durnerin, Braun, Fage, Paton, Michel, Schlesinger, Mules, Vernon, Reynolds, Weber and Ginsberg.

In cases of internal ophthalmoplegia following herpes zoster, in addition to sensory loss, certain motor fibers are involved. In these cases the lesion must be in the ciliary ganglion. Bar, in 1925, reported the case of a man aged 30 with partial paralysis of the third nerve, involving fibers to the pupil and the levator muscle. Being of the opinion that herpes zoster was an infectious neuritis due to a specific organism, he traced the association of the third and the fifth cranial nerves to their connection by a communication in the region of their entrance to the orbit. Cases of internal ophthalmoplegia have been described by Rutter, Achard and Castaigne, Baranov,



Elliot, Aurand, Veil and others Isolated paralysis of the pupils is frequently encountered and may be the only symptom The pupil is dilated and does not react to light or in accommodation to distance In a certain number of cases, involvement of the entire internal musculature is noted, and patients present, in addition to paralysis of the pupil, a paralysis of accommodation which impairs close vision In these cases of paralysis of accommodation and paralytic mydriasis the disturbance may persist for a long time Several hypotheses have been adduced in explanation of this association—among them, the conception of herpes zoster as an infectious ganglionic radiculitis, the implication of a meningeal reaction as an etiologic factor and the recognition of the intimate relationship between the virus of herpes and that of encephalitis, with frequent assumption of participation of lesions of polio-encephalitis in the production of these paralyzes Cases of paralysis of accommodation and paralytic mydriasis were reported by von Arlt, Beiln, Grandmont and Hofer Horner and Hasner reported cases of isolated paralysis of accommodation, and Oettinger, Cohn and D Sulzer each added a case of isolated paralytic mydriasis

Only one branch of the third nerve may be involved that which supplies the levator palpebrae muscle, and ptosis may result Usually recovery occurs Such cases of isolated paralysis have been reported, among others, by Blachez, Brissaud, Hutchinson, Balñia and Herrera, Tardy, Howard, Kirsaua and Wangler Study of a series of cases reveals a number of such cases of isolated paralysis In most instances unilateral ptosis on the same side as the eruption represents the initial symptom of paralysis Rarely both levator palpebral muscles are implicated at the same time, if so, ptosis is more prominent on the side of the eruption Ginsberg, Fouchard, Menacho, Cohn and Jacksch have reported cases Valude and Gallois, in 1924 published a case of bilateral ptosis and paralysis of the left superior rectus muscle in a woman aged 78 In a case described by Brissard the ptosis was associated with hemiplegia The ptosis came on several months after the vesicles and was permanent Letulle cited a case of ptosis which preceded the herpes zoster by two weeks

#### THIRD FOURTH AND SIXTH CRANIAL NERVES

Numerous cases of paralysis of the third, fourth and sixth nerves simultaneously have been recorded Voisin, in 1936 reported a case of a woman aged 73 in which the third, fourth and sixth cranial nerves were involved The right eye was proptosed, and motions were limited in

all directions Contributions to the literature have been cited by Rebattu, Kuhn, Monnier, Decbaume, Bonnet and Isrel Vázquez Barrière, in 1937, described a case of paralysis of these nerves in a man of 72 years After the cutaneous lesions had cleared, some exophthalmos was noted, followed by complete ophthalmoplegia and complete facial paralysis Seven months after the attack the ocular motility became normal and the facial paralysis disappeared Similar cases have been described by Sellers, Königstein, D Sulzer, Tacke, Barrett and Orr, Ginsberg, Hall, Silcock and Aubineau In the case described by Mildemberger, in 1937, the first and second branches of the fifth nerve were involved Dalsgaard-Nielsen, in 1935, reported a case of ophthalmoplegia complicated with acute glaucoma in a woman Francois, in 1936, observed a case in which ptosis was present from the onset The pupil was dilated and fixed, with no reaction to light or in accommodation Similar cases have been recorded by Head, Patterson, Turner, Velter, Leplat, Vazquez Barriere, Batignani, Pergola and Viallefont In the case reported by Higgins, the ophthalmoplegia came on ten weeks after the cutaneous eruption Brissaud cited a similar case in which the ophthalmoplegia followed the eruption in three months This author found that total paralysis of the ocular muscles occurred in 40 cases

#### SIXTH CRANIAL NERVE

Paralyses of the abducens nerve are intermediate in frequency between paralyses of the third and those of the fourth cervical nerve and usually appear a short time after the cutaneous eruption Metz, in 1913, found that paralysis of the sixth nerve occurred in 8 of 50 collected cases of paralysis of the ocular muscles Hunt found it in 6 of 24 cases of such paralyses Numerous other cases have been recorded in the literature by Doggart, McCulloch, Stieren, Galezowski and Beauvois, Danielson, Peter, Paton, Patterson, Gosetti, Weidner Langenhan, Raynard, Heydemann, Oliver, Goldschmidt, Heilbrun, Lockwood, Schiffer and others I found paralysis of the sixth nerve in 47 cases

#### FOURTH CRANIAL NERVE

Isolated transitory paralysis of the trochlear nerve represents a rare complication in the course of cephalic zoster However, Traquair cited 5 cases of such a complication, and Metz, 4 cases Other cases have been described by Hunt, Caspar, Silcock, Vogel, Sulzer, Grand, Lesser and others A total of 21 cases of paralysis of the fourth nerve were found in the literature

### INVOLVEMENT OF FIRST AND SECOND BRANCHES OF FIFTH CRANIAL NERVE

Up to the present time, there have been reported 72 cases of involvement of the first and second branches of the fifth cranial nerve. The first cases were reported by Hutchinson, in 1865, and by Bowman, in 1867, and since that time many cases of this condition have been described in patients of various ages, males and females alike. In many of these cases there was a history of complications involving the globe and the ocular muscles. Cases have been reported by Chance, Head, Flemming, Hunt, van Lint, Caspar, LaChaise, Bryan, Caire, Halipre, Schumacher, Bradshaw, Jaclard, Fassbender, Passera, Eyer, Lauber, Duplay, Cohn, Chemolosoft, Johnen, Horstmann, Knowles, Ramond, Ginetous and others. In a series of 98 cases of ophthalmic zoster, Hybord found 8 in which the superior maxillary branch was involved. Pergola described a case of involvement of the first and second branches of the fifth nerve in a man, a typographer, with paralysis of the levator palpebrae, iridocyclitis, hyphemia and complete ophthalmoplegia, followed by glaucoma. Pergola stated the belief that the lead from the type was carried through the blood stream and had affected the gasserian ganglion, and that the inflammatory process had traveled upward, to produce a lesion of the mesencephalon. Mildenerger and Bézi described similar cases. Fourestier and Zangger each reported a case of bilateral involvement. Langenhan, in 1910, reported a case of involvement of these branches complicated by paralysis of the sixth nerve. Smith, in 1878, cited a case complicated with hypopyon, with eventual loss of the eye. Sicard, in 1905, observed a case following mumps. According to van Lint's statement, in 1927, "Rene LaChaise, in his Lyons thesis, of 1924, was able to assemble only 26 cases of this condition," but I have found 56 cases in the literature up to that date.

When the eruption is limited to two branches, it is the adjacent branch that is always involved. No case has been observed in which two remote nerve trunks such as the ophthalmic and the inferior maxillary division, have been affected. Zoster involving two branches is known as partial trigemellar zoster.

### INVOLVEMENT OF FIRST, SECOND AND THIRD BRANCHES OF FIFTH NERVE

Involvement of all three branches of the gasserian ganglion is occasionally reported. Twenty-five cases of such a disorder are described in the

literature. The first case was reported by Schiffer and Wyss, in 1866. In cases of total trigemellar zoster, the ophthalmic, the superior maxillary and the inferior maxillary branch are involved, but there is also participation of the sympathetic ganglions, as evidenced by pupillary disturbances and enophthalmos. Head reported a case in which all three branches were involved, affecting both lids, the cheek, the mucous membrane of the cheek, the tongue and the tonsil. Other cases have been reported by Agnello, Vaughan, Gowers, Camus, Elliot, During and Huber, Murzin, Siméon and Denizet, and Bal-denweck and Degorce. Zentmayer, in 1906, cited a case in which all three branches of the fifth nerve were involved, complicated with muscular paralysis. Similar cases were reported by Roelofs, Pergola, Paton and Scriven. E. Rollet and associates, in 1931, described a case of paralytic mydriasis in a girl of 10 years. R. M. Campbell, in 1936, reported a case in which there was bilateral involvement of all three branches of the fifth nerve in a boy aged 6 years. Campbell stated that there were 30 instances of bilateral herpes zoster in the literature to date, but that the fifth nerve was not affected in all cases. Cases were reported by Glaubersohn, Fordyce, Fox, Hutton, Burgess and Anderson. Spicer, in 1892, cited a case of severe zoster resulting in keloid changes in the skin and in perforation of the globe. In the case reported by Murphy, facial paralysis was present. Gerson, in 1937, reported a case in which the zoster followed arsenical treatment. Griffith, in 1901, described a case of zoster in a man of 60 years in which all three branches of the right fifth nerve were involved. The eruption followed the course of the supratrochlear and the nasal branch of the ophthalmic nerve. Vesicles appeared also over the right malar bone, the upper lip and the chin, involving the temporo-malar branch of the superior maxillary nerve, the labial branches of the infraorbital nerve and the mental branch of the dental nerve. The eye was congested, with vesicles in the lower cul-de-sac and edema of the lids. The cornea was cloudy and ulcerated, with iritis and posterior synechias. Teulieres and associates, in 1933, described a similar case and concluded that involvement of the internal nasal nerve was always accompanied with lesions of the cornea.

### BILATERAL HERPES ZOSTER OPHTHALMICUS

Jeffries, in 1874, was the first to report a case of bilateral herpes zoster ophthalmicus, in a woman of 64 years. Both corneas were affected,

and perforation of the cornea resulted on each side

The disease is rarely bilateral, but other cases have been observed by Lallier, Samelsohn, Jaclard, Douglas, Lipschutz, Schiess-Gemuseus, von Barenprung, Hebra, Thomas and Buckley, Jorissenne, Greenough, Myers, Grindon, Carré and others. Touraine and Baumgartner, in 1934, reported a case of bilateral herpes zoster ophthalmicus in a man of 56 years. The nasal branch was not involved, and the cornea was free, but the frontal and lacrimal branches were affected on each side. Similar cases were reported by Verco, Blachez, Sedan, Anderson, Jaclard, Foustier, Fassbender, Tacke, Zangger and others. De River and Moore saw cases in persons with histories of syphilis. Gallois described a case of bilateral ptosis. Hallam, in 1897, reported a case of bilateral ophthalmic zoster in a girl aged 13 years. Kreibitz in 1938, treated a patient with severe bilateral herpes zoster ophthalmicus, which was followed by death in two days. G. A. Sulzer reported another case of severe ophthalmic zoster which resulted in bilateral optic neuritis. Habran, in 1877, described an interesting case of the disease in a pregnant woman aged 28 years. At the end of the ninth month of pregnancy pneumonia developed. Eight days after the termination of labor, typical bilateral herpes zoster ophthalmicus developed, involving the first and second branches of the fifth nerve. I found 44 cases of bilateral ophthalmic zoster in the literature.

#### RECURRENT HERPES ZOSTER OPHTHALMICUS

As a rule the disease occurs but once in a lifetime, but in some cases it has appeared more than once in the same person. Charcot, in 1859, published an account of the first case of recurrent herpes zoster ophthalmicus, in this case the disease followed a gunshot wound. Emmert, in 1870, reported 3 cases, 1 of a girl of 4 years. Carré, in 1875, described a case of ophthalmic zoster in a girl of 16 years with six recurrences on one side during a period of six months. The disease later became bilateral. Kaposi reported a case in which the eruption appeared five times within a comparatively short time. Drouet, in 1924, cited a case in a woman aged 54 with three recurrences in a period of eight weeks. In Niden's case four recurrences occurred in a period of six years. Cases in which the same nerve has been affected more than once have been reported by Berger, Fox, Kopp, Jaksch, Singer, Couyba, Talko, D. Sulzer, Spaeth, Hermann, Cofler, Grindon, Cookson, Vorner, Cross,

Hallam and others. Head and Campbell found 4 instances of recurrence in 400 cases. In several cases recurrence has resulted in enucleation, as described by Greenwood, Meller and others. Rollet and Colrat, in 1923, described the case of a man aged 45 who suffered from successive monthly eruptions of zoster in the territory of the left ophthalmic nerve. The ocular tension was 9 mm. The case was presented on account of the ophthalmomalacia associated with the ophthalmic zoster, which is a rare complication.

#### INVOLVEMENT OF THE OPTIC NERVE

The disease sometimes affects the deep membranes of the eye, and cases have been described by many observers in which retinal hemorrhage and degenerative retinitis, choroiditis, optic neuritis, papillitis, optic nerve atrophy and retrobulbar neuritis were present. In some cases, however, no previous ophthalmoscopic examination had been made, and it is questionable in these cases whether the lesions were secondary to the zoster or were present before the attack. However, inflammation of the optic nerve may complicate herpes zoster ophthalmicus and may manifest itself when the eruption appears or as an end result. It is postnueritic in type and may or may not heal without resulting atrophy.

The insidious character of herpes zoster ophthalmicus is apparent at times in optic neuritis, which develops with the characteristics of papillitis and may terminate in blindness or in great reduction of vision. This complication may be the only one observed in the course of the disease. An edematous neuritis is seen, and the disk has poorly defined contours. The vessels are congested and tortuous. The disk gradually becomes pale. The neuritis is more often localized in the eye on the side of the eruption, although both eyes may be affected.

Hebra, in 1870, was the first to report a case of bilateral optic nerve atrophy following herpes zoster. In this case delirium and diffuse encephalitis finally developed. Hubsch, in 1872, described a case of optic nerve atrophy in a man aged 52, who for many years had had chronic herpes zoster. Eruptions had appeared and disappeared in various parts of the body for a long time. Eventually there was a gradual diminution in vision in each eye, with subsequent optic nerve atrophy, which was ascribed to the papillitis, as a result of the continuous zoster. Coppez, in 1873, was the first to mention a case of opacities in the vitreous following herpes zoster, with choroiditis and retinitis. Later cases were described by Noyes, Tacke, Sattler and Haltenhoff.

Rollet and Colrat reported a case of optic nerve atrophy in a woman aged 70 years. There was paralysis of the left oculomotor nerve with marked papillitis, which they stated was caused by perichiasmal meningitis, although the papillitis was unilateral. Similar cases have been described in the literature by Gould, Sulzer, Bowman, Daguene, Wangler, Paton, Veasey, Adams, Strzeminski, Sinclair and others. Aurand, in 1920, described a case of optic neuritis in a woman aged 75 which he concluded was due to an embolus or a thrombus of the central retinal artery. Absence of cardiac lesions warranted the assumption of obliterating endarteritis. He stated the belief that circulatory disturbances in the territory of the ophthalmic branch facilitated localization of obliterating endarteritis. He mentioned 2 other instances of occurrence of vascular lesions in association with herpes zoster recorded by Andrieu-Thomas and Heuyer, in 1912. Pierson stated the belief that the optic nerve atrophy and optic neuritis were attributable to strangulation in the vicinity of the scleral ring.

Cohn cited a case of optic neuritis which developed after healing of the cutaneous lesions. After three months there was a small concentric contraction of the visual fields, with some reduction of vision. Cabannes reported a case of optic neuritis in a man of 30 years. The fundus was pale, the arteries were small, the veins were engorged, and two small, flame-shaped hemorrhages were noted near the disk. Other such cases have been noted in the literature by Murzin, Antonelli, Lohlein, Hirschberg and Puech. Ahlstrom encountered 1 case of optic neuritis among 50 cases of ophthalmic zoster. Koch, in 1939, reported a case in a child aged 5 years, with retinal edema and exudates in the macular region. Silcock mentioned 2 cases of optic neuritis, with retinal hemorrhages in 1 and thrombosis of the retinal vein in the other. Genet reported a case in which the condition resulted in phthisis bulbi, and Scott saw a case in which complete retinal detachment occurred.

Focosi, in 1935, described a case of retrobulbar neuritis with a large central scotoma, which developed during the course of ophthalmic zoster. He attributed the neuritis to the zoster because the neuritis manifested itself in the same region and occurred simultaneously with the zoster and because the herpetic process provoked lesions of other parts of the eye—in the cornea and the iris. He expressed the belief that the process was transmitted by branches of the trigeminal nerve which reach the optic nerve by way of the ophthalmic ganglion. This hypothesis was

enunciated by Fage Deutschmann, in 1924, reported a case in which large central scotoma was present and vision was limited to 1/200. Two months later atrophy of the nerve developed. The disk was pale and well defined. Serologic tests gave negative reactions. The teeth and sinuses were normal. The author concluded that the retrobulbar neuritis was herpetic and that the virus migrated from the nerve sheaths of the fifth nerve through the orbit to the optic nerve. Peter stated the belief that the neuritis was an extension of the herpetic toxemia from the uveal tract. The pathogenesis of neural involvement is still a matter of dispute.

#### INVOLVEMENT OF OTHER NERVES

Just as there are paralyzes of parts at a distance in cases of herpes zoster, irrespective of the situation of the eruption, so motor nerves of the eye may be affected in the course of zoster of remote localization. Most unusual are the cases in which wide separation exists between the areas involved. It is probable that two ganglions are affected at the same time. Delens and Wangler cited cases in which ophthalmic zoster followed or preceded zoster in other regions. Morénas and Colrat observed a case of paralysis of the extraocular muscles which occurred during the evolution of a dorsolumbar zoster. A woman aged 65 years suffered from zoster in the inferior thoracic region on the right side. One month later she complained of diplopia. Examination revealed total paralysis of the right third nerve. The zoster pains and the ocular paralysis persisted until her death. They stated the opinion that a nuclear origin of the paralysis in question might be assumed. Bradshaw, in 1894, described a case of thoracic zoster in a man aged 42 years, who at the same time had a zoster eruption on the left side of the head, with vesicles of the upper lid and conjunctiva. Hutchinson reported a similar case. Barber, in 1919, saw an interesting case in a child of 6 years who entered the hospital with herpes zoster on the left side of the chest. Two days later a similar eruption developed on the forehead, lid and temple of the same side. Corson and Knowles reported a case of a woman in which an outbreak of zoster occurred over the right scapula and at the same time an eruption developed over the first branch of the right ophthalmic nerve. Ahlstrom, Anger and Buller each described similar cases.

Hemiplegia of peduncular or alternate type is likewise encountered. G. A. Sulzer, in 1907, reported a case of zoster with paralysis of all the extraocular muscles. A few weeks later hemi-

plegia developed on the right side. The muscular paralysis soon recovered, but paralysis of the sphincter of the iris remained. Ironside, in 1933, described a case of a woman with corneal ulcer. Five weeks later right hemiplegia developed. MacGillivray, in 1931, saw a woman with ptosis and conjunctival injection following ophthalmic zoster. Three weeks later she complained of weakness in the right arm. There was no exaggeration of knee jerks, and Kernig's sign was absent. Later left hemiplegia developed. Wohlwill, Brissaud, Dumery, Grandclement and Chauffard and Rendu described similar cases. Peirce, Kissel, Pierquin and Gayet reported a case of zoster complicated with hemiplegia in a man aged 68 years. Autohemotherapy was used, whereupon the vesicles dried up and became covered with crusts and then disappeared, leaving deep cicatrices. The erythema in the frontal area persisted and was complicated with pronounced supraorbital and palpebral edema. Pains became intensified, and diplopia followed. Three weeks after the onset progressive left hemiplegia developed. The paralytic symptoms of the left arm and leg required eight days to become established. Paralysis of the left side of the face of central type followed. The authors stated the belief that the coexistence of ophthalmic zoster and hemiplegia was due to an exclusive radiculoganglionic lesion and that it warranted the establishment of the theory of zosterian neuritis. They concluded that in certain subjects who present vascular fragility the virus of zoster might provoke the occurrence of hemiplegia, though incapable of doing so in the healthy subject.

In some cases zoster is distributed over several adjacent segments while only one spinal ganglion is involved, no doubt owing to the presence of communicating fibers. At times the disease may affect widely separated areas simultaneously. Couyba, in 1877, described a case of a man aged 65 in which the disease ended fatally. In this case there was involvement of the trigeminal, glossopharyngeal, facial, spinal accessory and hypoglossal nerves. Dennis reported a case in which the fifth, seventh, eighth and ninth cranial nerves were involved. Powell, and Baldenweck and Degorce described similar cases. Claude and Schaeffer saw a case in which involvement of the third, fifth, sixth, seventh and eighth nerves followed ophthalmic zoster. The authors stated the belief that the primary process was an acute poliomyelitis posterior, which spread to involve the spinal ganglions and their analogues in the brain stem, the gasserian and geniculate ganglions. The extension from sensory to motor nuclei occurs through the spread of a basilar infection by way of the subarachnoid space, a meningitic process being demonstrated by the leukocytosis of the spinal fluid.

#### FATAL CASES

In cases of ophthalmic zoster disastrous consequences sometimes follow this usually mild infection, to the extent not only of complete destruction of the eye but even of death. Many observers have reported a fatal outcome, among them Weidner, Wagner, Wyss Aubineau, Brissaud, Doggart, Sunde, Bezi, Couyba, Howard and Wohlwill.

*(To Be Concluded)*

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

## Cornea and Sclera

KERATOCONUS POSTICUS CIRCUMSCRIPTUS G  
WISE, Am J Ophth 27:1406 (Dec) 1944

Wise reports a case of keratoconus posticus circumscriptus in a man aged 24. The lesion appeared as a large, eccentric, nebulous opacity, occupying more than one-half the corneal area posteriorly. The anterior surface showed a normal curvature. The interesting features of the case were that the cornea was one-fourth the normal thickness and that the lesion stopped short of the limbus.

W S REESE

CORNEAL DYSTROPHIES R VON DER HEYDT,  
Am J Ophth 28:55 (Jan) 1945

Von der Heydt briefly describes "Bueckler's triad" of corneal dystrophies which includes the Fleischer, the Haab-Dimmer and the Groenouw and also describes Fuchs's epithelial, and Salzmann's nodular dystrophies and keratonus.

W S REESE

THE USE OF CHOLINE IN CASES OF ULCER  
AND OF LEUKOMA OF THE CORNEA T J  
DIMITRY and P AZAR, Am J Ophth 28:62  
(Jan) 1945

Dimitry and Azar conclude that choline is a most promising agent in the treatment of ulcer and leukoma of the cornea and that it should be applied topically.

W S REESE

A CASE OF CORNEA PLANA C COCKBURN,  
Brit J Ophth 28:486 (Oct) 1944

The condition of cornea plana was seen in a Greek soldier, aged 28. Visual acuity had always been poor, although, significantly, he stated that it had deteriorated since enlistment, one year previously. The refractive error for the right eye was  $+10.50$  D sph  $\subset +1.50$  D cyl, axis 60, with visual acuity of 6/36, and the error for the left eye was  $+12$  D sph  $\subset +1.00$  D cyl, axis 90, with visual acuity of 6/60. The right cornea was clear, the left cornea had a fairly dense central nebula. The family history was negative for the condition.

Comparison of photographs of the normal eye with photographs of the eye with cornea plana showed that the affected globe was approximately of normal size, the cornea was definitely smaller than normal, the line of corneoscleral junction had lost its sharp definition and the

curvature of the cornea was the same as that of the sclera.

W ZENTMAYER

FILAMENTOUS KERATITIS AND KERATOCONJUNCTIVITIS SICCA J MALBRAN and A ARRECHEA, Arch de oftal de Buenos Aires 18:603 (Nov) 1943

The so-called filamentous, or filiform, keratitis is hard to classify as a distinct nosologic entity. Its etiopathologic features are obscure, many factors having been mentioned in its causation. Formerly it was thought that the filaments were only coagulated fibrin deposits in the cornea. Later a degenerative process of the corneal epithelium was said to be the cause. Still later it was stated that the keratitis was produced by diminished lacrimal secretion or dryness of the cornea. It was also said that the condition might exist in healthy corneas or might follow corneal ulceration or operation, and that it could also be produced by systemic conditions or disease.

The condition known as keratitis sicca is produced by a decrease or absence of lacrimal secretion, and "filaments" are at times noted.

The Sjogren syndrome of keratoconjunctivitis sicca, a general disease involving also the lacrimal glands and producing dryness of the cornea and conjunctiva, is not related to the disease discussed. If keratoconjunctivitis sicca is really a nosologic entity, there are cases of deficient lacrimal secretion accompanied with filamentous formations which could be classified with typical filamentous keratitis.

The following etiologic classification of lacrimal hyposecretion is accepted: congenital, traumatic or postoperative and spontaneous.

Without asserting that all the cases of filamentous keratitis in the literature are related to keratoconjunctivitis sicca, the authors express the belief that they probably are.

"Filamentous keratitis is a particular state of lacrimal hyposecretion or complete absence of tears, and it manifests itself under circumstances which are difficult to explain at present. The lacrimal hyposecretion is produced by diverse etiopathogenic mechanisms, but in all cases the condition could be classified as keratoconjunctivitis sicca."

To diagnose the condition, the Schirmer test should be used to determine the extent of the lacrimal section, and the slit lamp is necessary to visualize the corneal changes. Good results were obtained with ocular occlusion in 1 case,



and with Rucker's formula (a mixture of gelatin and Locke's solution) in another

H F CARRASQUILLO

### Experimental Pathology

EFFECT OF RETINAL EXTRACTS ON GROWTH OF BLINDED MALE RATS L G BROWMAN and A A BROWMAN, *Proc Soc Exper Biol & Med* 57 171 (Nov) 1944

The evidence is consistent that total ablation of both eyes retards growth and sexual maturity in rats. It is possible that the eye exerts its influence on the pituitary gland, which, in turn, produces growth and gonadotropic substances. The interaction between the eye and the pituitary gland may be either through direct or indirect neural connections between the eye and the pituitary body or through a humoral mechanism. The present investigation is based on the hypothesis that a humoral mechanism is elaborated by the eyes of normal mammals which is necessary for normal growth and sexual maturity. Of the various retinal extracts of bovine retinas used by the authors, only the saline preparation yielded suggestive results in the direction of alleviating the retardation of weight and delayed sexual maturity characteristic of blinded male rats.

P C KRONFELD

### General Diseases

ASSOCIATION BETWEEN RETINOPATHIES AND ENCEPHALOPATHIES IN THE COMMON CARDIO-VASCULO-RENAL AFFECTIONS D J LYLE, *Am J Ophth* 27:1232 (Nov) 1944

This article, the author's thesis for membership in the American Ophthalmological Society, does not lend itself to abstracting. It has a number of good illustrations and two charts presenting the findings in the retina, heart, kidneys and urine in 41 cases.

W S REESE

OCULAR SIGNS OF RIBOFLAVIN DEFICIENCY W J W FERGUSON, *Lancet* 1:431 (April) 1944

Sydenstricker and his associates in 1940 described ocular signs and symptoms which responded to riboflavin therapy. The symptoms were photophobia, sensations of burning or roughness of the eyelids, visual fatigue and sometimes impairment of visual acuity in the absence of refractive errors or pathologic changes in the media. The commonest sign was "circumcorneal injection," often with invasion of the cornea by capillaries from the limbic plexus. Ferguson examined groups of patients with the slit lamp and discussed and made examinations in cases with Sydenstricker. He feels that misinterpretation has arisen largely through lack of

experience in the use of the slit lamp, through imperfect understanding of the normal variations in the appearance and vascularity of the limbus and through inclusion of cases of corneal vascularization due to causes other than riboflavin deficiency. The mode of anastomosis of the anterior and posterior conjunctival vessels around a normal limbus varies. There are four typical varieties, which demonstrate that formation of capillary loops at the corneoscleral junction and on the limbus itself may be regarded as normal. The vascularization attributed to lack of riboflavin is an extension of the normal limbic vascular system to the true cornea. From the apexes of the existing limbic loops fine vessels run more or less toward the true cornea, these "streamers," in turn, anastomose with one another to form other loops, from which more streamers and, in turn, loops may be formed. The true cornea may thus become increasingly vascularized. These vessels run superficially, immediately under the epithelium, and are of such small caliber that they are usually invisible even with an ordinary binocular loupe. With the corneal microscope and slit lamp they show best when observed with light reflected from the iris, and they may readily be missed with direct corneal illumination. Abnormal corneal vascularization with very mild symptoms was found in 78 per cent of 422 persons. In 13 patients in whom the effect of riboflavin treatment was studied over an adequate period therapy resulted in cessation of the abnormal corneal circulation. No claim is made that riboflavin deficiency is the only cause of the corneal condition described.

J A M A (W ZENTMAYER)

OCULAR COMPLICATIONS IN BRUCELLOSIS RODOLFO LAJE WESHAMP, ROQUE A MAFRAND and MANUEL J PEIROTTI, *Arch de oftal de Buenos Aires* 18:666 (Dec) 1943

The authors discuss this serious disease, which they consider a menace in their country. The malady is widespread, especially so in the northwestern region of Argentina, where a great number of goats, cattle and hogs appear to be contaminated.

In two years the authors have observed over 50 cases in 35 per cent of which ocular complications were present. The authors found that the optic nerve is frequently involved. Edema of the disk, probably the result of acute or chronic meningoencephalitis produced by the infection, is the commonest complication. At times true congestion of the papilla or optic neuritis occurs. Isolated retinal hemorrhages are occasionally seen. Muscular paralyses, most commonly of the lateral rectus muscles, the result of basilar meningitis, are present at times. Ocular examination revealed a normal condition in 12 cases.

The authors give in detail the history and observations in the cases they studied and summarize the cases reported in the literature

H F CARRASQUILLO

# Hygiene, Sociology, Education and History

EDWARD JACKSON'S PLACE IN THE HISTORY OF REFRACTION W H CRISP, *Am J Ophth* 28: 1 (Jan ) 1945

Crisp gives a historical outline of refraction and enumerates the various papers and contributions of Jackson to this subject

W S REESE

## Injuries

THE MANAGEMENT OF TRAUMATIC HYPIHEMIA R O RACHENER J A M A 126: 762 (Nov 18) 1944

The author in association with Ellett, has seen in the past eighteen years 9 patients with traumatic hyphemia, all in consultation weeks and months after blood staining and secondary glaucoma had occurred, and in none of them was any useful vision restored, even though the cornea cleared. The injured eye of 4 patients had to be removed because of intractable pain or unsightly appearance, in 1 of these patients sympathetic ophthalmitis developed and the sympathizing eye was lost. Two cases illustrating different phases of traumatic hyphemia are given. The following conclusions are reached

"Traumatic hyphemia may be controlled by simple paracentesis of the cornea and the instillation of miotics

"Surgery should be accomplished without delay whenever the intraocular pressure is increased or no clear aqueous is visible in the anterior chamber

"It is possible that the use of miotics rather than mydiatics immediately after injury will result in less secondary hemorrhages and less necessity for surgical procedures "

W ZENTMAYER

SNAKE VENOM OPHTHALMIA H RIDLEY, *Brit J Ophth* 28: 568 (Nov ) 1944

This interesting article describes spitting snakes, together with an account of the composition and action of snake venom in general, a report of a case of snake venom ophthalmia and a discussion of the therapeutic uses of venom

A man aged 30 was cutting long grass in Africa with a native "scythe," when a concealed black-necked cobra raised its head and forcibly spat venom, some of which entered the patient's right eye. When he was seen twenty minutes after the injury, there was moderate conjunctival injection, with edema of the entire corneal epithelium

The lower two thirds of the cornea was opaque and showed punctate staining with fluorescein, as did two semicircular areas at the periphery of the cornea in the interpalpebral area. Sensation was absent from the cornea and remained so for five to seven days. On the fifth day the cornea was completely covered with edematous, loosely attached epithelium, which formed a pyramidal elevation. On the eleventh day the epithelium was removed, revealing an opacity in Bowman's membrane. On the fourteenth day the eye had completely recovered. Visual acuity was 6/6. There were no general toxic symptoms. A corneal opacity was present two months later.

W ZENTMAYER

## Lens

THE PRODUCTION OF LENS SENSITIVITY IN RABBITS BY BRUCELLA INFECTION E L BURKY, *Am J Ophth* 27: 1394 (Dec ) 1944

Burky's experiments suggest that lens sensitization can be produced by infecting a damaged lens. They do not suggest that the brucella is the offending organism, although recent observations on patients with ocular disease indicate that it may occasionally be the sensitizing agent

W S REESE

EXTRACTION OF SENILE CATARACT W F HUGHES and W C OWENS, *Am J Ophth* 28: 40 (Jan ) 1945

Hughes and Owens summarize their results and draw the following conclusions

"The gradual but radical changes in the technique of extraction of uncomplicated senile cataract during the past 19 years at the Wilmer Institute have brought about a steady improvement in final results. Statistical analysis of 2,086 extractions has shown that (1) the amount of lens capsule and cortex remaining after an extracapsular extraction is directly related to the development of postoperative iridocyclitis, which, in turn, is the main factor in the production of secondary glaucoma, (2) loss of vitreous predisposes to postoperative simple detachment of the retina, persistent vitreous opacities, and iridocyclitis, (3) corneoscleral sutures reduce the incidence of incomplete closure of the wound, prolapse of iris, the amount of final astigmatism, and, with two sutures, anterior-chamber hemorrhages, (4) preservation of the round pupil reduces the likelihood of vitreous loss, (5) diabetes of long standing or requiring 30 units of insulin or more per day predisposes to the development of severe anterior-chamber hemorrhages, but there is no correlation between the height of the bloodsugar and postoperative complications, (6) syphilis, either treated or untreated, and systemic hypertension have no significant influence on the occurrence of postoperative complications "

W S REESE



## Lids

RECONSTRUCTION OF THE LOWER LID BY  
HUGHES' METHOD J FOSTER, Brit J  
Ophth 28: 515 (Oct) 1944

Foster reports 2 cases of basal cell carcinoma of the lower lid, unsuitable for irradiation, in which the procedure described by Hughes was employed. In the first case the final step of the operation could not be carried out, as the patient met with accidental death. In the second case the general cosmetic and functional results were satisfactory.

The article is illustrated W ZENTMAYER

CONGENITAL ECTROPION ASSOCIATED WITH  
BILATERAL PTOSIS CASE REPORT S  
GORDON, Brit J Ophth 28: 520 (Oct)  
1944

Gordon reports a case of congenital ectropion of all four lids, with associated ptosis of the upper lids. The facial bones were normal. A satisfactory correction of the defects was obtained by inserting into each upper lid a thin Thiersch graft cut from the arm and into the lower lids a Wolfe graft of postauricular skin. Four months later facial slings attaching the upper lids to the frontalis muscle overcame the ptosis.

The article is illustrated W ZENTMAYER

PTOSIS V D SATHAYE, Indian J Ophth 4: 54  
(July) 1943

In a case of bilateral ptosis it is necessary to know whether the levator muscle is completely, or only partially, paralyzed and whether there is only paresis of Muller's muscle.

In a case of monocular ptosis it is essential to determine whether the condition is real or apparent. Paralysis of the superior rectus muscle of one eye with a spasm of the inferior oblique muscle of the affected eye may give the appearance of ptosis. The differentiation can be made by holding up both upper lids and asking the patient to close the eyes firmly. Normally the eyes will roll up in so doing.

W ZENTMAYER

## Neurology

TUBEROUS SCLEROSIS M D SACHS and D A  
SHASKAN, Am J Roentgenol 52: 35 (July)  
1944

According to Sachs and Shaskan, tuberous sclerosis is a rare hereditary disease of ectodermal origin. Tuberous sclerosis, Recklinghausen's neurofibromatosis and trigeminal nevus with angioma of the brain are distinct neurocutaneous syndromes. Of the three, tuberous sclerosis presents the most clearcut clinical,

roentgenologic and pathologic picture. It is most frequently associated with mental retardation and epileptic seizures. The authors describe a case of tuberous sclerosis in a white soldier aged 32. The cardinal findings in this case, with a history of epileptic seizures, were adenoma sebaceum, fibromatous nodules on the forehead, scalp and back, a pigmented, hairy nevus of the lumbar area, vitiligo of the left thigh and the left side of the back, phacomia of the retina, and 'cotton ball' calcifications of the brain, right greater trochanter and fifth lumbar vertebra. The authors think that delay in the diagnosis of tuberous sclerosis is probably due to the physician's unfamiliarity with the syndrome because of its comparative rarity.

J A M A (W ZENTMAYER)

NEUROSYPHILIS AND THE OCULIST A C  
ESPOSITO, M Bull Vet Admin 21: 51  
(July) 1944

Esposito describes the routine for examination of the eyes followed at Chillicothe, Ohio. The confrontation test for the field of vision is found satisfactory, and especially suited to the more deteriorated type of patients.

In the series of 218 patients with neurosyphilis, 14 had on preliminary examination some impairment, such as optic nerve atrophy, field defects or failing vision, which contraindicated trypanamide therapy, of the remaining 204 patients who were placed under treatment with trypanamide, symptoms of drug toxicity involving the optic nerve developed in 26. The author reaches the following conclusions:

All patients with neurosyphilis should be referred to the oculist before their treatment is begun. Each such patient should be returned for examination of the visual fields, central vision and fundi after each of the first ten injections of trypanamide during the first and each subsequent course of treatment. Administration of trypanamide should be permanently discontinued at the first sign of a toxic reaction involving the optic nerve. Malaria therapy, with later treatment with trivalent arsenical and bismuth preparations, should be instituted for the patients showing reactions.

W ZENTMAYER

## Ocular Muscles

REPAIR FOLLOWING TUCKING OPERATIONS ON  
THE EXTRAOCULAR MUSCLES K S  
CHOUKE, Am J Ophth 28: 50 (Jan) 1945

Chouke gives the following summary:

"After a tucking operation the two adjacent sides of the loop of muscle join together by means of fibrous connective tissue. The side of the muscle nearest the eyeball quite often, but not always, becomes attached to the sclera by fibrous connective tissue. The process of repair of

extraocular muscles in the dog is essentially similar to that of the skeletal muscles elsewhere in the body. The time required for the completion of repair of extraocular muscles is slightly longer than that for general skeletal muscles of the same animal. The continuity of the muscle is preserved after the tucking operation, as evidenced by response to electrical stimulation."

W S REESE

DEFINITION OF ANOMALOUS RETINAL CORRESPONDENCE K C SWAN, *Am J Ophth* 28: 58 (Jan) 1945

Swan summarizes his discussion as follows

"The prevalent definition of abnormal retinal correspondence as an anomaly in which the fovea of the fixating eye and a peripheral retinal area in the squinting eye become functionally corresponding points seems erroneous. Studies of the field of binocular vision reveal that the peripheral retinal area in question is almost invariably suppressed.

"Unless there is a high degree of amblyopia the macular region of the squinting eye is only partially suppressed, consequently, demonstration that the foveal or macular regions of the two eyes are not corresponding points provides a practical method of diagnosing anomalous retinal correspondence in the great majority of patients. Afterimages, stereoscopic devices, or a filter projection system may be utilized to stimulate the macular regions and to determine their relative visual directions.

"Anomalous retinal correspondence is not necessarily fixed at a constant angle of anomaly, but is frequently variable and tends to adapt itself to the deviation of the eyes. Experience with several hundred cases indicates that instead of completely disrupting abnormal retinal correspondence, muscle surgery alone usually results in a gradual change in the angle of anomaly to correspond with the new deviation.

"Another characteristic of anomalous retinal correspondence is that it becomes unstable with disuse, that is, disruption of binocular vision. Prolonged monocular occlusion is an important adjunct in treatment of the anomaly.

"In accordance with these findings, anomalous retinal correspondence is defined as an anomaly of binocular vision in which areas in the two retinas normally having a common visual direction—for example, the foveas—acquire an unstable and often variable visual direction in relation to each other but usually in accordance with the squinting position. The anomaly is always associated with some degree of suppression of the squinting eye, the point of fixation almost invariably being viewed monocularly."

W S REESE

## Orbit, Eyeball and Accessory Sinuses

AN OPERATION FOR SHRUNKEN SOCKET J KRAUS, *Brit J Ophth* 28: 224 (April) 1944.

The operation consists essentially in a dissection of the conjunctiva from the floor of the orbit, the implanting of a skin graft and the use of a cavity dilator which produces a circular force from within outward. The space between the margins of the lids remains unaltered, and the maximum pressure is exerted well within the socket, with diminishing force along the retractor blade, toward the lid margins. The steps of the operation are well illustrated in the article.

W ZENTMAYER

MUCOCELE OF MAXILLARY ANTRUM G E DODDS, *Brit J Ophth* 28: 510 (Oct) 1944

The condition was observed in a Nigerian native. A swelling was situated just above the lower margin of the orbit and could be palpated for a certain distance into the orbit. It gave the typical sensation of a fluid-containing cyst and was but slightly movable from side to side. The globe was displaced upward. Definite proof that the diagnosis was mucocele of the antrum has not so far been obtained in this case.

The article is illustrated W. ZENTMAYER.

## Retina and Optic Nerve

OBSTRUCTION OF THE CENTRAL RETINAL VEIN. B A KLIEN, *Am J Ophth* 27: 1339 (Dec.) 1944

Klien attempts to correlate clinical and histopathologic data in this study. She presents 17 cases and concludes that primary phlebosclerosis plays a greater role in venous occlusion than has heretofore been supposed. The site of the most extensive proliferative endophlebitis is frequently the anterior lamina cribrosa. Anticoagulant and antispasmodic therapy gives more promise for the younger patients.

W S REESE

OPHTHALMOSCOPIC CLASSIFICATION OF HYPERTENSIVE DISEASES G E CLAY and M BAIRD, *Am J Ophth* 27: 1396 (Dec) 1944.

Clay and Baird discuss hypertension and outline a classification. They conclude that the greatest need is that of a commission to formulate a proper nomenclature and classification of hypertensive disease.

W S REESE

CLINICAL STUDIES IN ANGIOSPASM I GIVNER, *Am J Ophth* 27: 1408 (Dec) 1944

Givner presents 3 cases of angiospasm, each representative of a type. He discusses these cases from the standpoint of prognosis and diagnosis and suggests that future investigations in

such cases include pupillographic studies to gain information as to the part the hypothalamus plays

W S REESE

### Tumors

BILATERAL METASTATIC CARCINOMA OF THE CHOROID WITH X-RAY THERAPY IN ONE EYE F C CORDES, *Am J Ophth* 27 1355 (Dec) 1944

Cordes gives the following summary

"1 A case is reported of a woman, aged 31 years who had bilateral metastasis to the choroid secondary to a scirrhous carcinoma of the breast

"2 One eye was enucleated and the diagnosis confirmed by microscopic examination

"3 With the appearance of a similar growth in the second eye x-ray irradiation was employed. This was followed by disappearance of the tumor and retention of 20/20 vision in the eye. Fourteen months later there was a recurrence. The eye was again irradiated, with regression of the tumor

"4 Employing x-ray therapy to the eye made it possible for the patient to retain 20/20 vision up to the time of death (23 months)

"5 While the ultimate prognosis is hopeless, the possibility of retaining useful vision by means of palliative irradiation should receive consideration in cases of metastatic carcinoma of the choroid"

W S REESE

DIAGNOSIS OF ORBITAL TUMORS W L BENEDICT, *J A M A* 126 880 (Dec 2) 1944

This is the address of the guest of honor of the Section on Ophthalmology of the American Medical Association read at the Ninety-Fourth Annual Session

The article does not lend itself to abstraction and should be read in the original. Benedict supplies the following summary and conclusions

"The probability of tumor in any case of exophthalmos is so great that only in cases of goiter is there serious doubt of the presence of an expanding lesion. The temptation to explore the orbit is irresistible for some surgeons and an exploration is planned. This is not a surgical procedure but a diagnostic one unless the surgeon is prepared to remove the tumor and do the necessary repair. Exploration by trocar is useless and should never be done. Such a procedure is of no help in diagnosis, and in case of malignant tumor or vascular aneurysm it is positively dangerous. Puncture for digital exploration only should never be practiced. One cannot explore the orbit with the finger from any one place along the rim and be sure that nothing has been missed. Exploration of the orbit for diagnosis should always be done through an incision large enough and so placed that, should a tumor be encoun-

tered or any other pathologic condition be found that would require surgical removal, the operation can be completed at the time. If one is not sure of the presence of a tumor, it is in most instances safe to employ roentgen therapy and await developments"

W ZENTMAYER

THE GENETICS OF RETINOBLASTOMA A D GRIFFITH and A SORSBY, *Brit J Ophth* 28: 279, 1944

At the Royal Eye Hospital, London, 59 children with retinoblastoma were seen between 1894 and 1943. Only one familial group has now been observed over three generations, with 6 cases of the disease. The condition was bilateral in 15.1 per cent of cases.

Analysis of the literature shows that the mode of inheritance is irregularly dominant. The incidence of bilateral involvement appears to be higher for the genetic type of retinoblastoma than for the sporadic type. It is possible that hereditary retinoblastoma is a distinct histologic entity, differing from the sporadic types.

W ZENTMAYER

UNILATERAL AND BILATERAL RETINOBLASTOMA A POSSIBLE HISTOLOGICAL DIFFERENCE J W CUMMINGS and A SORSBY, *Brit J Ophth* 28 533 (Nov) 1944

In an attempt to answer the question whether genetic retinoblastoma is histologically different from the sporadic variety, the authors studied 21 cases. Two cases were excluded as instances of unusual tumor formation. The remaining 19 cases consisted of 8 instances of unilateral retinoblastoma, 8 instances of bilateral retinoblastoma and 3 cases of hereditary retinoblastomas. From the study it is suggested that unilateral retinoblastoma originates in the outer nuclear layer, while the bilateral tumors are derived from both nuclear layers or, possibly less frequently, from the inner nuclear layer. In the 3 cases of hereditary retinoblastoma the tumors were bilateral and did not appear to differ from the sporadic bilateral retinoblastoma.

The article is illustrated W ZENTMAYER

### Uvea

GONORRHOEAL IRIDO-CYCLITIS TREATED BY PENICILLIN, WITH REPORT OF A CASE A J ELLIOT, *Canad M A J* 51 257, 1944

A man aged 28 was treated for acute gonorrheal urethritis and secondary gonorrheal arthritis with sulfadiazine. On the eleventh day of treatment administration of the drug was discontinued because of the presence of casts in the urine. During the time of treatment iridocyclitis developed in the right eye. The iris was bound down by posterior synechias. After unsuccessful efforts to free the synechias with sub-

conjunctival injections of a solution containing epinephrine hydrochloride (1:4,000), cocaine hydrochloride and atropine sulfate, treatment with injection of 500 units of penicillin through the cornea was given for five days, together with intravenous injections of penicillin, in a dose of 15,000 units every three hours. Local application of atropine was continued, at the end of this time the pupil was widely dilated and vision had improved from perception of hand movements only to 20/15. The arthritis did not respond to the penicillin therapy.

W ZENTMAYER

### Vision

AMBLYOPIA IN CASES OF READING FAILURE  
T H EAMES, *Am J Ophth* 27:1374  
(Dec) 1944

Eames gives the following summary

"The records of 100 cases of reading failure were compared with those of an equal number of children who were known to be passing in their school studies. A considerably greater incidence of amblyopia was found among the poor readers, and they exhibited a greater average amount of amblyopia in the left eye only. The average amount of amblyopia in the right eye only and in both eyes was the same in each group."

W S REESE

THE EFFECT OF THE DURATION OF STIMULUS  
ON THRESHOLD MEASUREMENTS IN THE  
DARK ADAPTED EYE S YUDKIN, *Brit J*  
*Ophth* 28:611 (Dec) 1944

Yudkin describes the instrument used and the method of carrying out the test and supplies the following summary and conclusions

Five groups of 60 to 115 men were tested on each of three occasions. The thresholds for the dark-adapted rods of all the men were measured, using a test light exposed in flashes of 0.2 second's duration. In addition, the thresholds for the men in each group were tested with a light exposed in flashes of one of the following durations: 0.02, 0.04, 0.1, 0.5 and 1 second.

The following results were obtained

The mean threshold was lower for the longer durations up to 0.5 second, but the lowering of the threshold was not proportional to the increased duration of exposure. The range of thresholds for all the groups was the same whatever the exposure. The variability of individual thresholds from test to test was least with the 0.2 second exposure.

The results given here are probably applicable to all measurements of threshold made with similar instruments

W ZENTMAYER

### Vitreous

CYSTIC FORMATIONS IN THE VITREOUS BODY  
A CLINICAL CASE JOSE SAENZ CANALES,  
*An Soc mex de oftal y oto-rino-laring*  
17:123 (July-Aug) 1942

Canales refers to this anomaly as an ophthalmologic curiosity since it is rarely seen by the oculist, as it does not alter the normal condition of the eye and the patient does not seek medical advice unless some intercurrent condition is present.

The following classification of cysts of the vitreous is made: cysts located in the anterior part of the vitreous, near the crystalline lens; cysts located in the posterior part of the vitreous, in the vicinity of the optic disk, and cysts free in the vitreous body.

Of the first type the following subtypes are considered: (1) cysts produced by anterior remains of the fetal hyaloid vascular system, a lesion which may or may not be associated with opacities in the crystalline lens; cysts produced by remains of the anterior portion of the canal of Cloquet, and cysts of ciliary origin, which may be congenital or acquired.

Of the second type the following subtypes are defined: cysts formed by posterior remains of the fetal hyaloid vascular system, cysts representing the posterior remains of the canal of Cloquet, cysts formed by mesodermal remains of the fetal cleft, and cysts of uveal origin, which may be congenital or acquired.

Of the third type, two subtypes, congenital and acquired, are described.

Detailed descriptions of the appearance of all these cysts are given, and numerous citations from the literature are made. The differential diagnosis is well discussed.

The author reports a clinical case. A patient aged 32 complained of poor vision for distance, which was worse in the right eye. Visual acuity in the left eye was 7/10 and could be improved to 8/10 with the pinhole disk, in the right eye it was 4/10 and could not be improved. Both eyes showed opacities in the vitreous, as well as well defined, disseminated pigmentary changes in the retinas; a cystic formation was observed in the region of the papilla in the right eye. The author diagnosed the lesion as a cyst of the vitreous and classified it as a cyst formed by the posterior remains of the fetal hyaloid vascular system. The pigmentary changes he believed to be hereditary, probably syphilitic. General physical examination revealed nothing significant.

H F CARRASQUILLO

# Society Transactions

EDITED BY DR W L BENEDICT

## COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

WARREN S REESE, M.D., *Chairman*

GEORGE F J KELLY, M.D., *Clerk*

*April 19, 1945*

### Conservation of Lid Margins During Blepharoplasty DR CHARLES A RANKIN

The author presented the history and treatment of a white boy aged 17 years. The middle half of one upper lid had been cut away by flying metal in an explosion in a chemical laboratory. Particles of lid margin were reunited by dovetailing. Further and complete reconstruction of the lid with use of skin and mucous membrane grafts was carried out. The final result showed a well conserved, smooth, even lid margin, with no notching or overcorrection. The cilia were well placed.

#### DISCUSSION

DR EDMUND B SPAETH. Much good plastic work on the eyes has been spoiled by an attempt "to gild the lily." It is as important to know when not to operate further as to know when to operate and what to do.

Essex, Wiener, Wheeler and others have written much on the conservation of lid margins in ophthalmic plastic work. Elsching and Snellen both spoke many years ago of dovetailing separate flaps. As far as I know, the case presented by Dr Rankin is the first instance of separate attention to the margin of the lid and to that portion of the lid above the margin. It is a procedure which can be utilized basically in many traumatic lacerations of the lid. I am sure.

DR JAMES S SHIPMAN. I think there are no operations performed about the eye by the general hospital intern that cause more harm and lead to more plastic repair in the future than those on wounds of the eyelid. Fortunately, this patient was seen at the start by some one who realized the seriousness of the condition. I think we ophthalmologists who are associated with general hospitals can do much to prevent the necessity of future plastic repair by instructing the general intern to refrain from sewing up the eyelid when the laceration goes through the margin of the lid.

### Angioid Streaks Observed over a Period of Thirty-Six Years. Report of a Case DR WILLIAM ZENTMAYER

In the case of angioid streaks first observed by Dr Zentmayer in 1908 and seen at varying intervals since, the last time in May 1944, the right eye showed masses of dense pigment of irregular shapes. In some portions of the fundus there was complete atrophy of the choroid. The gray zone which was formerly observed about the papilla had disappeared, and there was no longer any trace of angioid streaks. The papilla was somewhat waxy in appearance.

In the left eye the general appearance of the fundus was similar to that of the right eye, only the areas of complete destruction of the choroid were more extensive and there was denser massing of pigment. Beneath the superior temporal retinal artery there was a vertical lesion, about 3 disk diameters in length which had the appearance of the lesions associated with cicatricial retinitis. The papilla was waxy in appearance.

Vision was 1/60 in each eye. The patient had suffered a stroke affecting his speech. The systolic blood pressure was 210 mm of mercury.

The condition of angioid streaks is probably due to degeneration of Bruch's membrane, with which tearing is associated, and the hemorrhages result from similar changes in the walls of the blood vessels. All other changes in the fundus are a part of the syndrome. The association with pseudoxanthoma elasticum occurs with such frequency that it may be assumed that the two conditions have a common pathologic basis.

### Factors in the Examination of Astigmatism DR I S TASSMAN

Certain difficulties are sometimes encountered in the accurate determination of the kind and amount of astigmatism and also in the exact determination of the axis of the correcting cylinder. Probably for this reason a great deal of stress is laid on procedures and tests for making these determinations by subjective examination. The examination and correction of ametropia cannot be reduced simply to a single mathematical or mechanical procedure. Important factors in the examination of the patient include a proper and thorough analysis and evaluation of the subjective symptoms. Such symptoms include headache, dizziness, double vision and blurring. Whenever these symptoms are complained of, it should first be determined whether they are



the result of, or are associated with, ametropia, particularly astigmatism

Hyperopic astigmatism causes more discomfort than myopic astigmatism, except when the latter is of low degree. The amount of accommodative effort employed is an important factor in the production of symptoms in cases of hyperopic astigmatism. It is also an important factor in cases of convergent strabismus. In the latter, the deviating eye invariably presents a greater amount of hyperopic astigmatism, usually at an oblique axis, while in the fixing eye there may be little, if any, astigmatism.

In young children with fairly high hyperopic astigmatism in one eye and little, if any, astigmatism in the other eye, amblyopia may occur very early, whether or not a deviation is present. In most cases of astigmatism in young children of early school age symptoms and complaints may be absent. In older children and in young and middle-aged adults, subjective symptoms resulting from the presence of hyperopic astigmatism are more common. In very old patients who use the eyes only moderately for close work, a considerable degree of astigmatism may be present without troublesome symptoms. The occupation of the patient, the accommodation and the type of astigmatism bear an important relationship to the presence of symptoms. Young people who do close work constantly and who have hyperopic astigmatism which requires the use of a great deal of accommodation will usually complain of headache and ocular fatigue.

A cycloplegic should be employed in refraction with all young patients. In all cases of astigmatism, whether a cycloplegic is employed or not, retinoscopy should provide the basic determination of the refractive error and the axis of astigmatism. The best method for this purpose is what is known as "cylinder retinoscopy," at 1 meter. However, whether spherical or cylindric retinoscopy is used, the preliminary determination by either method should not be neglected. In cases of irregular astigmatism with corneal opacities, scissors motions, immature changes in the lens and other alterations in the media, difficulties may be encountered in obtaining an accurate result with retinoscopic tests. In these cases retinoscopic examination at a closer distance is recommended to obtain the best possible result.

In cases in which a cycloplegic is used the subjective test should follow the objective test, and in cases of average astigmatism the results should correspond. In young children the result of a careful retinoscopic examination is more dependable than the result of a subjective test, and it is arrived at in a much shorter time. Post-cycloplegic examination should follow the cycloplegic test. This should provide the final result. Here, the cross cylinder can be employed in some cases as an auxiliary in checking the axis of the cylinder and the strength of the combina-

tion. The astigmatic dial can also be employed as an auxiliary or as a preliminary test with some selected patients, but it does not eliminate the need for careful retinoscopic tests in routine practice.

#### DISCUSSION

DR ALFRED COWAN. I should like to emphasize what Dr. Tassman said about the procedure known as cylinder retinoscopy. This is probably the most accurate objective test known for persons for whom one has to depend entirely on objective tests. It is the only way to determine objectively the amount of astigmatism and the axis of the cylinder.

I agree with Dr. Tassman here, but I do not agree that the importance of the subjective examination should not be overemphasized. I do not think one can overemphasize its importance. After all, in cases in which one can make a subjective test, the subjective test is all-important. No objective test can be conclusive, no matter how well it is done or by whom. With the subjective test one can probably come nearest to the exact refraction.

DR I. S. TASSMAN. I think that today much emphasis is placed on subjective tests while other important factors and the objective examination are more or less neglected. As I stated in the paper, the subjective test provides the final result, but I am afraid that there has been a tendency during the past few years, in the examination of many patients to underestimate and neglect the objective tests. Dr. Cowan stated that "with the subjective test one can probably come nearest to the exact refraction." This depends a great deal on the intelligence and power of discrimination of the patient, which are frequently found to be lacking. I also mentioned such factors as the accommodation, the age and occupation of the patient and the nature of the symptoms as important in properly recognizing and evaluating the nature of the condition present.

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#### NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

THOMAS H. JOHNSON, M.D., *Chairman*

WENDELL L. HUGHES, M.D., *Secretary*

March 19, 1945

#### Toxoplasmosis: Report of Two Cases DR RAYMOND L. PFEIFFER

Toxoplasmosis should be considered in the etiologic study of chorioretinal disease. The possibility of toxoplasmosis constitutes another indication for roentgenography in cases of suspected retinoblastoma.

#### DISCUSSION

DR FERDINAND L. KOCH. It is gratifying to learn from Dr. Pfeiffer's excellent report that

other examiners are finding the diagnosis of toxoplasmosis warranted in certain instances Drs Wolf, Cowen, Paige and I after our original report on the ocular findings in this protozoal entity, almost doubted for a time whether we had seen any of these lesions. We knew very well, of course, that we had, but few others appeared to find them.

Since we did not wish to be too enthusiastic, publication of our report was delayed for more than a year in order to confirm and recheck the individual diagnoses by serologic tests on those patients who had not come to autopsy. One should, however, be conservative in making a diagnosis of toxoplasmosis merely on the basis of the serologic results.

DR RALPH I LLOYD In 1890, Lindsay Johnson described a group of cases of a condition which he named extrapapillary coloboma, to distinguish it from the type connected with defective closure of the optic fissure. The features noted were a sharp, clearcut margin with normal surrounding tissue, pigment anterior to the vessels and irregular pigmented lines against the bare sclera. Since then, Treacher Collins, Ida Mann and Arnold Sorsby have studied cases both clinically and microscopically. Collins and Sorsby describe the condition as a defective development of the choroid, while Ida Mann states that it is the result of intrauterine inflammation. Ida Mann divides the disease into three types: that with pigment border and pigment against the sclera, that with ectasia of the sclera, and that with vessels of the ciliary or the choroidal region emerging from a defect and ramifying in the retina. She gives a different date of origin for each type: the second month of gestation, for the last type, the fourth to the fifth month, for the second type, and the sixth month, for the first type. Other arguments for the congenital origin of the defect is that it runs in families and that the mixing of retinal vessels with the other types is not duplicated in disease. Clinical experience has taught the necessity of differentiating these defects from healed tuberculosis of the choroid and from a type of hereditary macular degeneration. Now that toxoplasmosis has been studied and defects of the fundus shown to be part of the disease which are similar to some previously considered as congenital, an effort should be made to review past experience and determine whether this form known as extrapapillary coloboma should be subdivided. That lesions of this type could be the result of choroidal disease in infancy does not seem possible to me. On the other hand, the claim that this disease can exist in the embryo and damage the developing eye cannot be dismissed without careful consideration. It does seem that these defects must be prenatal in origin because of associated errors of development found in some cases, like apical dystrophy of the phalanges, malformations of facial bones, retinal folds, choroidal defects about the optic

disk and pigment clumps scattered throughout the fundus.

DR ARNOLD KNAPP Apparently, in all cases in children, areas of calcification in the brain were demonstrable in the roentgenograms of the skull. I should like to ask Dr Pfeiffer whether these calcifications are also found in defective or premature infants when this lesion of the retina is not present.

I think the most interesting part of the presentation is the suggestion that toxoplasmosis occurs in adults and that the diagnosis can be made from the ophthalmoscopic picture. I feel that one should be hesitant in making this diagnosis, because, as Dr Pfeiffer says, the roentgenograms of the skull in adults are negative and the diagnosis can be confirmed only by a serologic test, which, as far as I know, is still not definitely accepted.

DR RAYMOND L PFEIFFER In answer to Dr Knapp's questions. Few premature babies have been studied roentgenographically in my laboratory, so that I cannot speak from personal experience. I should think, however, that one ought not to expect to find these deposits of calcium in the brain of a child simply because it is premature. So many children with toxoplasmosis are born prematurely, and, certainly, the finding of these deposits, with their irregular and strange distribution, which does not follow any particular order and may be found anywhere throughout the brain substance, is strong evidence of toxoplasmosis. In fact I think one can make the statement, as I already have, that the co-existence of these deposits and the ocular findings described is diagnostic of toxoplasmosis. As I explained, the serologic test has not as yet been fully evaluated, so that the diagnosis of toxoplasmosis in an adult is still open to question.

#### **Clinical Differentiation of Emboli in the Retinal Arteries and Endarteritis** DR ARTHUR J BEDELL

This article will be published in full in a future issue of the ARCHIVES.

#### **Paralysis of Elevation with Real Blepharoptosis and Pseudoblepharoptosis** DR DANIEL B KIRBY

This article will be published in full with discussion in a later issue of the ARCHIVES.

#### **The Surgical Limbus** DR HENRY MINSKY

The difficulties in choosing properly the site of the keratome section in operations for glaucoma are due to the inherent obscuration of the angle of the anterior chamber by the scleral overhang which forms the anatomic limbus of the cornea. Since this overhang varies in different persons, no numerical designation is always adequate.



Most surgeons enter the anterior chamber too far forward, thereby failing to deliver the root of the iris into the wound. When the iridectomy is performed, a bridge of the iris tissue is left behind, as Reese has pointed out.

The surgical limbus, as opposed to the anatomic one, can be easily demonstrated by focal illumination of the corneal margin contralateral to the site of incision. If a focal beam of light is made to impinge on the limbus at 6 o'clock the upper limbus glows by internal reflection in the cornea. The outside margin of the glow on the sclera represents the projection of the hidden clear cornea. If the point of the keratome is placed at the periphery of the surgical limbus and entered into the eyeball in the plane of the iris it will reach the angle of the anterior chamber.

Anatomic evidence was presented in slides to show the relationship of the limbic glow to the angle of the anterior chamber. A microscopic slide showed that the tract of the keratome wound when made in this way, was placed just in front of the base of the iris.

Two photographs of an intercalary rupture of the cornea with prolapse of the iris were shown. The first, as usually taken, the second, demonstrating the glow of the surgical limbus. The prolapse was precisely at the outer margin of the surgical limbus, proving the validity of the experimental work.

The practical importance of this method is found in the security the surgeon feels when he makes his incision in cataract extraction in the Lagrange operation and in basal iridectomy.

## News and Notes

EDITED BY DR W L BENEDICT

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### GENERAL NEWS

**Ophthalmological Society of Mexico and College of Medicine of National University of Mexico**—On joint invitation from the Ophthalmological Society of Mexico and the College of Medicine of the National University of Mexico, Dr Daniel B Kirby, of New York, gave a series of lectures and surgical clinics in Mexico, D F. The lectures were given at the Cardiology Institute, and the surgical clinics were held at the Hospital de la Luz, April 16 to 27 inclusive. Forty-five Mexican ophthalmologists attended the course, at the completion of which the dean of the College of Medicine and the rector of the university made Dr Kirby an honorary professor of ophthalmology.

**Sociedade de Oftalmologia de Minas Geraes**—The Sociedade de Oftalmologia de Minas Geraes on April 7, at the São Geraldo Hospital, elected the following officers for the

year 1945-1946: president, Dr Geraldo Queroga, vice president, Dr Amelio Bonfiohi, secretary, Dr Guilherme Fonseca, treasurer, Dr Helio Faria.

**Sociedade de Oftalmologia de São Paulo.**—The Sociedade de Oftalmologia de São Paulo elected the following officers for 1945-1946: president, Dr Silvio de Almeida Toledo, vice president, Dr Penido Burnier Filho, general secretary, Dr Plinio Toledo Piza, secretary, Dr Moacir Cunha, treasurer, Dr Aureliano Fonseca, filing, Dr Orlando Aprighiano.

**New York Academy of Medicine, Section of Ophthalmology**—The new officers of the section are:

Chairman: Dr Rudolf Aebli, 30 East Fortieth Street, New York; secretary: Dr Truman L Boyes, 654 Madison Ave, New York.

The meetings will be held at 8 30 p m, on the third Monday of every month from October to May, inclusive.

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## Book Reviews

### **Modern Ophthalmic Lenses and Optical Glass**

By Theodore E Obrig. Third edition. Price \$4.50. Pp 323, with 180 illustrations, charts and tables. Philadelphia: The Chilton Company, 1944.

This excellent treatise was fully reviewed in the ARCHIVES (14: 315 [Aug] 1935) when it first appeared, in the same year. The third edition is fully revised and includes improvements in optical glass and in spectacle lenses and a description of contact lenses, telescopic spectacles and newer types of bifocals. These are all sub-

jects of practical importance to the ophthalmologist. The book is an up-to-date treatise and contains information which is important and often difficult to acquire. For this the author has placed the reader in his debt, and many will find this manual instructive and useful.

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### CORRECTION

In the article by Dr Charles A Bahn entitled "Ophthalmic Requirements of the Military Services: Changes from Jan 1, 1944 to Jan 1, 1945," which appeared in the March issue (ARCH OPHTH 33: 245, 1945), the table on page 245 should have appeared under that section of the article entitled "C Air Corps Flying."

# Directory of Ophthalmologic Societies \*

## INTERNATIONAL

### INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President Dr P Baillart, 66 Boulevard Saint-Michel,  
Paris, 6<sup>e</sup>, France

Secretary-General Prof M Van Duyse, Université de  
Gand, Gand, Prov Ostflandern, Belgium

All correspondence should be addressed to the Secre-  
tariat, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France

### INTERNATIONAL OPHTHALMOLOGIC CONGRESS

President Prof Nordenson, Serafimerlasarettet, Stock-  
holm, Sweden

Secretary Dr Ehlers, Jerbanenegade 41, Copenhagen,  
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Executive Secretaries Dr Conrad Berens, 35 E 70th  
St, New York Dr M E Alvaro, 1511 Rua Con-  
solacão, São Paulo, Brazil

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Hospital, Bangalore

Secretary Dr G Zachariah, Flitcham, Marshall's Rd,  
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London, W 1

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President Dr H T Pi, Peiping Union Medical Col-  
lege, Peiping

Secretary Dr C K Lin, 180 Hsi-Lo-yen Chienmeng,  
Peiping

Place Peiping Union Medical College, Peiping Time  
Last Friday of each month

### FACULTY OF OPHTHALMOLOGISTS

President Brig Sir Stewart Duke-Elder, 63 Harley  
St, London, W 1, England

Secretary Mr Frank W Law, 45 Lincoln's Inn  
Fields, London, W C 2, England

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All correspondence should be addressed to the Assistant  
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Birmingham 3, England

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Place Manchester, Bradford, Leeds, Newcastle-upon-  
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October to April

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Sydney

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### OPHTHALMOLOGICAL SOCIETY OF EGYPT

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ment Hospital, Alexandria

Secretary Dr Mohammed Khalil, 4 Baehler St, Cairo

All correspondence should be addressed to the secretary,  
Dr Mohammed Khalil

### OPHTHALMOLOGICAL SOCIETY OF SOUTH AFRICA

President Dr A W Sichel, National Mutual Bldg,  
Church Square, Cape Town

Secretary Dr J K de Kock, Groote Kerk Bldg, 32  
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Secretary Dr H D Dastur, Dadar, Bombay 14, India

Place H B A Free Ophthalmic Hospital, Parel,  
Bombay 12 Time First Friday of every month

### OXFORD OPHTHALMOLOGICAL CONGRESS

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W 1, England

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\* Secretaries of societies are requested to furnish the  
information necessary to make this list complete and  
keep it up to date

## POLISH OPHTHALMOLOGICAL SOCIETY

President Dr W Kapuscinski, 2 Waly Batorego, Poznan  
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 Place Lindley'a 4, Warsaw

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 Secretary Dr Alexander Garrow, 15 Woodside Pl, Glasgow, C 3  
 Place Edinburgh and Glasgow, in rotation

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SOCIEDAD OFTALMOLOGIA DEL LITORAL,  
ROSARIO (ARGENTINA)

President Prof Dr Carlos Weskamp, Laprida 1159, Rosario  
 Secretary Dr Arturo Etchemendigaray, Villa Constitucion, Santa Fe  
 Place Rosario Time Last Saturday of every month, April to November All correspondence should be addressed to the President

## SOCIEDADE DE OFTALMOLOGIA DE MINAS GERAIS

President Prof Hilton Rocha, Rua Rio de Janeiro 2251, Bello Horizonte, Minas Geraes, Brazil  
 Secretary Dr Ennio Coscarelli, Rua Amores 1697, Bello Horizonte, Minas Geraes, Brazil

SOCIEDADE DE OFTALMOLOGIA E OTORRINOLARINGOLOGIA  
DE RIO GRANDE DO SUL

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LARYNGOLOGIA DA BAHIA

President Dr Theonilo Amorim, Barra Avenida, Bahia, Brazil  
 Secretary Dr Adroaldo de Alencar, Brazil  
 All correspondence should be addressed to the President

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 Secretary Prof Dott Epimaco Leonardi, Via del Gianicolo, 1, Rome

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 Secretary Dr Sadger Ma, 9 Bialik St, Tel Aviv, Palestine

## NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC  
ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman Dr Frederick C Cordes, 384 Post St, San Francisco  
 Secretary Dr R J Masters, 23 E Ohio St, Indianapolis  
 In compliance with the request of the Office of Defense Transportation and in the interest of the national war effort a meeting will not be held in 1945

AMERICAN ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President Dr Gordon B New, Mayo Clinic, Rochester, Minn  
 President-Elect Dr Alan C Woods, Johns Hopkins Hospital, Baltimore 5  
 Executive Secretary-Treasurer Dr William L Benedict, 100-1st Ave Bldg, Rochester, Minn

## AMERICAN OPHTHALMOLOGICAL SOCIETY

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 Secretary-Treasurer Dr Walter S Atkinson, 129 Clinton St, Watertown, N Y

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President Dr Alexander E MacDonald, 170 St George St, Toronto  
 Secretary-Treasurer Dr L J Sebert, 170 St George St, Toronto

## CANADIAN OPHTHALMOLOGICAL SOCIETY

President Dr R Evatt Mathers, 34½ Morris St, Halifax, N S  
 Secretary-Treasurer Dr Kenneth B Johnston, Suite 1, 1509 Sherbrooke St W, Montreal

NATIONAL SOCIETY FOR THE PREVENTION OF  
BLINDNESS

President Mr Mason H Bigelow, 1790 Broadway, New York  
 Secretary Miss Regina E Schneider, 1790 Broadway, New York  
 Executive Director Mrs Eleanor Brown Merrill, 1790 Broadway, New York

# SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY,  
SECTION ON EYE, EAR, NOSE AND THROAT  
President Dr N Zwaifler, 46 Wilbur Ave, Newark  
Secretary Dr William F Keim Jr, 25 Roseville Ave,  
Newark  
Place 91 Lincoln Park South, Newark Time 8 45  
p m, second Monday of each month, October to May

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY  
President Dr Watson Gailey, 1000 N Main St,  
Bloomington, Ill  
Secretary-Treasurer Dr William F Hubble, 861-867  
Citizens Bldg, Decatur, Ill

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY  
President Dr L J Friend, 425 E Grand Ave, Beloit,  
Wis  
Secretary Dr G L McCormick, 626 S Central Ave,  
Marshfield

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY  
President Dr Theodore L Terry, 140 Marlborough St,  
Boston  
Secretary-Treasurer Dr Merrill J King, 264 Beacon  
St, Boston  
Place Massachusetts Eye and Ear Infirmary, 243  
Charles St, Boston Time 8 p m, third Tuesday of  
each month from November to April, inclusive

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY  
President Dr D H O'Rourke, 1612 Tremont Pl,  
Denver  
Secretary-Treasurer Dr C Allen Dickey, 450 Sutter  
St, San Francisco

PUGET SOUND ACADEMY OF OPHTHALMOLOGY  
AND OTO-LARYNGOLOGY  
President Dr James H Mathews, 1317 Marion St,  
Seattle, Wash  
Secretary-Treasurer Dr Barton E Peden, 301 Stimson  
Bldg, Seattle 1  
Place Seattle or Tacoma, Wash Time Third Tues-  
day of each month except June, July and August

ROCK RIVER VALLEY EYE, EAR, NOSE AND  
THROAT SOCIETY  
President Dr J Sheldon Clark, 27 E Stephenson St,  
Freeport, Ill  
Secretary-Treasurer Dr Harry R Warner, 321 W  
State St, Rockford, Ill  
Place Rockford, Ill, or Janesville or Beloit, Wis  
Time Third Tuesday of each month from October  
to April, inclusive

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY  
President Dr L D Gomon, 308 Eddy Bldg, Saginaw,  
Mich  
Secretary-Treasurer Dr Harold H Heuser, 207  
Davidson Bldg, Bay City, Mich  
Place Saginaw or Bay City, Mich Time Second  
Tuesday of each month, except July, August and  
September

SIoux VALLEY EYE AND EAR ACADEMY  
President Dr J C Decker, 515 Francis Bldg, Sioux  
City, Iowa  
Secretary-Treasurer Dr J E Dvorak, 408 Davidson  
Bldg, Sioux City, Iowa

# SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

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San Antonio, Texas  
Secretary Dr J W Jervey Jr, 101 Church St,  
Greenville, S C

# SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President Dr H L Brehmer, 221 W Central Ave,  
Albuquerque, N Mex  
Secretary Dr A E Cruthirds, 1011 Professional Bldg,  
Phoenix, Ariz

# SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President Dr W M Dodge, 716 First National Bank  
Bldg, Battle Creek  
Secretary-Treasurer Dr Kenneth Lowe, 25 W Mich-  
igan Ave, Battle Creek  
Time Last Thursday of September, October, Novem-  
ber, March, April and May

# WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Ray Parker, 218 Franklin St, Johnston,  
Pa  
Secretary-Treasurer Dr J McClure Tyson, Deposit  
Nat'l Bank Bldg, DuBois

# STATE

# ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President Dr Raymond C Cook, 701 Main St, Little  
Rock  
Secretary Dr K W Cosgrove, Urquhart Bldg, Little  
Rock

# COLORADO OPHTHALMOLOGICAL SOCIETY

President Dr C A Ringle, 912-9th Ave, Greeley  
Secretary Dr W A Ohmart, 1102 Republic Bldg,  
Denver  
Place University Club, Denver Time 7 30 p m,  
third Saturday of each month, October to May, in-  
clusive

# CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President Dr F L Phillips, 405 Temple St, New  
Haven  
Secretary-Treasurer Dr W H Turnley, 1 Atlantic  
St, Stamford, Conn

# EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President William O Martin Jr, Doctors Bldg,  
Atlanta  
Secretary-Treasurer Dr C K. McLaughlin, 526  
Walton St, Macon

# INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr F McK Ruby, Union City  
Secretary Dr Edwin W Dyar Jr, 23 E Ohio St,  
Indianapolis  
Place French Lick Time First Wednesday in April

IOWA ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr J K Von Lackum, 117-3d St S E,  
Cedar Rapids  
Secretary-Treasurer Dr B M Merkel, 604 Locust St,  
Des Moines

KANSAS STATE MEDICAL SOCIETY, SECTION ON OPH-  
THALMOLOGY AND OTOLARYNGOLOGY

President Dr W D Pittman, Pratt  
Secretary Dr Louis R Haas, 902 N Broadway,  
Pittsburg

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND  
OTOLARYNGOLOGICAL SOCIETY

President Dr Val H Fuchs, 200 Carondelet St., New  
Orleans  
Secretary-Treasurer Dr Edley H Jones, 1301 Wash-  
ington St, Vicksburg, Miss

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF  
OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr Robert H Fraser, 25 W Michigan  
Ave, Battle Creek  
Secretary Dr R G Laird, 114 Fulton St, Grand  
Rapids

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr George E McGeary, 920 Medical Arts  
Bldg, Minneapolis  
Secretary Dr William A Kennedy, 372 St Peter St,  
St Paul  
Time Second Friday of each month from October to  
May

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President Dr William Morrison, 208 N Broadway,  
Billings  
Secretary Dr Fritz D Hurd, 309 Medical Arts Bldg,  
Great Falls

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OTOLARYNGOLOGY

President Dr W Howard Morrison, 1500 Medical  
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Lincoln

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON  
OPHTHALMOLOGY, OTOTOLOGY AND  
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Chairman Dr George P Meyer, 410 Haddon Ave,  
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Secretary Dr John P Brennan, 429 Cooper St,  
Camden

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR,  
NOSE AND THROAT SECTION

Chairman Dr Harold J Joy, 504 State Tower Bldg,  
Syracuse 2  
Secretary Dr Maxwell D Ryan, 660 Madison Ave,  
New York 21

NORTH CAROLINA EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr Hugh C Wolfe, 102 N Elm St,  
Greensboro  
Secretary Dr Vanderbilt F Couch, 104 W 4th St,  
Winston-Salem

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY  
AND OTO-LARYNGOLOGY

President Dr W L Diven, City National Bank Bldg,  
Bismarck  
Secretary-Treasurer Dr A E Spear, 20 W Villard,  
Dickenson

OREGON ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr Paul Neely, 1020 S W Taylor St,  
Portland  
Secretary-Treasurer Dr Lewis Jordon, 1020 S W  
Taylor St, Portland  
Place Good Samaritan Hospital, Portland Time  
Third Tuesday of each month

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr Lewis T Buckman, 83 S Franklin St,  
Wilkes-Barre  
Secretary Pro Tem Dr Paul C Craig, 232 N 5th  
St, Reading  
Time Last week in April

RHODE ISLAND OPHTHALMOLOGICAL AND  
OTOLOGICAL SOCIETY

Acting President Dr N Darrell Harvey, 112 Water-  
man St, Providence  
Secretary-Treasurer Dr Linley C Happ, 124 Water-  
man St, Providence  
Place Rhode Island Medical Society, Library, Provi-  
dence Time 8 30 p m, second Thursday in  
October, December, February and April

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr J L Sanders, 222 N Main St, Green-  
ville  
Secretary Dr J H Stokes, 125 W Cheves St,  
Florence

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr Wesley Wilkerson, 700 Church St,  
Nashville  
Secretary-Treasurer Dr W D Stinson, 124 Physicians  
and Surgeons Bldg, Memphis

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL  
SOCIETY

President Dr F H Rosebrough, 603 Navarro St,  
San Antonio  
Secretary Dr M K McCullough, 1717 Pacific Ave,  
Dallas

UTAH OPHTHALMOLOGICAL SOCIETY

President Dr R B Maw, 699 E South Temple, Salt  
Lake City  
Secretary-Treasurer Dr Charles Ruggeri Jr, 1120  
Boston Bldg, Salt Lake City  
Place University Club, Salt Lake City Time 7 00  
p m, third Monday of each month

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND  
OPHTHALMOLOGY

President Dr Mortimer H Williams, 30½ Franklin  
Rd S W, Roanoke  
Secretary-Treasurer Dr Meade Edmunds, 34 Franklin  
St, Petersburg

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE,  
EAR, NOSE AND THROAT SECTION  
President Dr George Traugh, 309 Cleveland Ave,  
Fairmont  
Secretary Dr Welch England, 621½ Market St,  
Parkersburg

### LOCAL

#### AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr E L Mather, 39 S Main St, Akron,  
Ohio  
Secretary-Treasurer Dr V C Malloy, 2d National  
Bank Bldg, Akron, Ohio  
Time First Monday in January, March, May and  
November

#### ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr B M Cline, 153 Peachtree St N E,  
Atlanta, Ga  
Acting Secretary Dr A V Hallum, 478 Peachtree  
St N E, Atlanta, Ga  
Place Grady Hospital Time 6 00 p m, fourth Mon-  
day of each month, from October to May

#### BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman Dr Ernst Bodenheimer, 1212 Eutaw Pl,  
Baltimore  
Secretary Dr Thomas R O'Rourke, 104 W Madison  
St, Baltimore  
Place Medical and Chirurgical Faculty, 1211 Cathedral  
St Time 8 30 p m, fourth Thursday of each  
month from October to March

#### BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President Each member, in alphabetical order  
Secretary Dr Luther E Wilson, 919 Woodward Bldg,  
Birmingham, Ala  
Place Tutwiler Hotel Time 6 30 p m, second  
Tuesday of each month, September to May, inclusive

#### BROOKLYN OPHTHALMOLOGICAL SOCIETY

President Dr Michael J Buonaguro, 589 Lorimer St,  
Brooklyn  
Secretary-Treasurer Dr Benjamin C Rosenthal, 140  
New York Ave, Brooklyn 16  
Place Kings County Medical Society Bldg, 1313 Bed-  
ford Ave Time Third Thursday in February, April,  
May, October and December

#### BUFFALO OPHTHALMOLOGIC CLUB

President Dr Walter F King, 519 Delaware Ave,  
Buffalo  
Secretary-Treasurer Dr Sheldon B Freeman, 196  
Linwood Ave, Buffalo  
Time Second Thursday of each month

#### CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Each member, in alphabetical order  
Secretary Dr Douglas Chamberlain, Chattanooga  
Bank Bldg, Chattanooga, Tenn  
Place Mountain City Club Time Second Thursday  
of each month from September to May

#### CHICAGO OPHTHALMOLOGICAL SOCIETY

President Dr Samuel J Meyer, 58 E Washington  
St, Chicago 2  
Secretary Dr W A Mann, 30 N Michigan Ave,  
Chicago 2  
Place Continental Hotel, 505 N Michigan Ave  
Time Third Monday of each month from October  
to May

#### CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman Dr D T Vail, 441 Vine St, Cincinnati  
Secretary Dr A A Levin, 441 Vine St, Cincinnati  
Place Cincinnati General Hospital Time 7 45 p m,  
third Friday of each month except June, July and  
August

#### CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman Dr M Paul Motto, Rose Bldg, Cleveland  
Secretary Dr H H Wygand, Guardian Bldg, Cleve-  
land  
Time Second Tuesday in October, December, February  
and April

#### COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman Dr W S Reese, 1901 Walnut St,  
Philadelphia  
Clerk Dr George F J Kelly, 37 S 20th St,  
Philadelphia  
Time Third Thursday of every month from October  
to April, inclusive

#### COLUMBUS OPHTHALMOLOGICAL AND OTO- LARYNGOLOGICAL SOCIETY

Chairman Dr Erwin W Troutman, 21 E State St,  
Columbus, Ohio  
Secretary-Treasurer Dr T Rees Williams, 380 E  
Town St, Columbus 15, Ohio  
Place University Club Time 6 15 p m, first Mon-  
day of each month, from October to May, inclusive

#### CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr C B Collins, 704 Medical Professional  
Bldg, Corpus Christi, Texas  
Secretary Dr L W O Janssen, 710 Medical Profes-  
sional Bldg, Corpus Christi, Texas.  
Time 6 30 p m, third Tuesday of each month from  
October to May

#### DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Ruby K Daniel, Medical Arts Bldg,  
Dallas 1, Texas  
Secretary Dr Tom Barr, Medical Arts Bldg, Dallas 1,  
Texas  
Place Dallas Athletic Club Time 6 30 p m, first  
Tuesday of each month from October to June The  
November, January and March meetings are devoted  
to clinical work



### DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr H C Schmitz, 604 Locust St, Des Moines, Iowa  
 Secretary-Treasurer Dr Byron M Merkel, 604 Locust St, Des Moines, Iowa  
 Time 7 45 p m, third Monday of every month from September to May

### DETROIT OPHTHALMOLOGICAL CLUB

Chairman Members rotate alphabetically  
 Secretary Dr Cecil W Lepard, 1025 David Whitney Bldg, Detroit 26  
 Place Club rooms of Wayne County Medical Society  
 Time First Wednesday of each month, November to April, inclusive

### DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Raymond S Goux, 545 David Whitney Bldg, Detroit 26  
 Secretary Dr Arthur Hale, 1609 Eaton Tower, Detroit 26  
 Place Club rooms of Wayne County Medical Society  
 Time 6 30 p m, third Thursday of each month from November to April, inclusive

### EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President Appointed at each meeting  
 Secretary-Treasurer Dr Joseph L Holohan, 330 State St, Albany  
 Time Third Wednesday in October, November, March, April, May and June

### FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Rex Howard, 602 W 10th St, Fort Worth, Texas  
 Secretary-Treasurer Dr R H Gough, Medical Arts Bldg, Fort Worth, Texas  
 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each month except July and August

### HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SECTION

President Dr Lyle J Logue, 1304 Walker Ave, Houston, Texas  
 Secretary Dr John T Stough, 803 Medical Arts Bldg, Houston, Texas  
 Place Medical Arts Bldg, Harris County Medical Society Rooms Time 8 p m, second Thursday of each month from September to June

### INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr Myron Harding, 23 E Ohio St, Indianapolis  
 Secretary Dr Kenneth L Craft, 23 E Ohio St, Indianapolis  
 Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each month from November to May

### KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo  
 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo  
 Time Third Thursday of each month from October to June The November, January and March meetings are devoted to clinical work

### LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Dennis Smith, 623 Security Bldg, Long Beach 2, Calif  
 Secretary-Treasurer Dr Robert Null, 710 Security Bldg, Long Beach 2, Calif  
 Place Seaside Hospital Time Last Wednesday of each month from October to May

### LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Orrie E Ghrist, 210 N Central Ave, Glendale, Calif  
 Secretary-Treasurer Dr K C Brandenburg, 110 Pine Ave, Long Beach 2, Calif  
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time 6 00 p m, fourth Monday of each month from September to May, inclusive

### LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky  
 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky  
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

### LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Each member in alphabetical order  
 Secretary Dr James J Monohan, 31 S Jardin St, Shenandoah, Pa

### MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr P S Constantinople, 1835 I St N W, Washington  
 Secretary Dr Frazier Williams, 1801 I St N W, Washington  
 Place 1718 M St N W Time 8 p m, third Friday of each month from October to April, inclusive

### MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Each member in alphabetical order  
 Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn  
 Place Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital Time 8 p m, second Tuesday of each month from September to May

### MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Ralph T Rank, 238 W Wisconsin Ave, Milwaukee  
 Secretary-Treasurer Dr Frank G Treskow, 411 E Mason St, Milwaukee 2  
 Place University Club Time 6 30 p m, fourth Tuesday of each month from October to May

## MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman Dr H V Dutrow, 1040 Fidelity Medical Bldg, Dayton, Ohio  
 Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio  
 Place Van Cleve Hotel Time 6 30 p m, first Tuesday of each month from October to June, inclusive,

## MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr J Rosenbaum, 1396 Ste Catherine St W, Montreal, Canada  
 Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada  
 Time Second Thursday of October, December, February and April

## NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr M M Cullom, 700 Church St, Nashville, Tenn  
 Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville, Tenn  
 Place St Thomas Hospital Time 8 p m, third Monday of each month from October to May

## NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President Dr William H Ryder, 185 Church St, New Haven, Conn  
 Secretary Dr Frederick A Wiess, 255 Bradley St, New Haven, Conn

## NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr W B Clark, 1012 American Bank Bldg, New Orleans  
 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans  
 Place Louisiana State University Medical Bldg Time 8 p m, second Tuesday of each month from October to May

## NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman Dr Thomas H Johnson, 30 W 59th St, New York  
 Secretary Dr Wendell L Hughes, 131 Fulton Ave, Hempstead, N Y  
 Time 8 30 p m, third Monday of every month from October to May, inclusive

## NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President Dr Maurice L Wieselthier, 117 E 30th St, New York  
 Secretary Dr Benjamin Esterman, 983 Park Ave, New York 28  
 Place New York Academy of Medicine, 2 E 103d St Time 8 p m, first Monday of each month from October to May, inclusive

## OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr James P Luton, 117 N Broadway, Oklahoma City  
 Secretary Dr Harvey O Randel, 117 N Broadway, Oklahoma City  
 Place University Hospital Time Second Tuesday of each month from September to May.

## OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President Dr D D Stonecypher, Nebraska City, Neb  
 Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha  
 Place Omaha Club, 20th and Douglas Sts, Omaha Time 6 p m dinner, 7 p m program, third Wednesday of each month from October to May

## PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President Dr Thomas Sanfacon, 340 Park Ave, Paterson, N J  
 Secretary-Treasurer Dr J Averbach, 435 Clinton Ave, Clinton, N J  
 Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every month, except June, July and August

## PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President Dr Isaac Tassman, 136 S 16th St, Philadelphia  
 Secretary Dr Glen Gregory Gibson, 255 S. 17th St, Philadelphia  
 Time First Thursday of each month from October to May

## PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President Dr George H Shuman, 351-5th Ave, Pittsburgh  
 Secretary Dr Robert J Billings, 509 Liberty Ave, Pittsburgh  
 Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each month, except June, July August and September

## READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Isaac B High, 326 N 5th St, Reading, Pa  
 Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa  
 Place Wyomissing Club Time 6 30 p m, third Wednesday of each month from September to July

## RICHMOND EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Luther C Brawner, Professional Bldg, Richmond, Va  
 Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va  
 Place Westmoreland Club Time 6 p m, second Monday of each month from October to May

## ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y  
 Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

## ST LOUIS OPHTHALMIC SOCIETY

President Dr Vincent Jones, 634 N Grand Blvd, St Louis  
 Secretary Dr T E Sanders, 508 N Grand Blvd, St Louis 3  
 Place Oscar Johnson Institute Time Fourth Friday of each month from October to April, inclusive, except December, at 8 00 p m

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL  
SOCIETY

President Dr Belvin Pritchett, 705 E Houston St,  
San Antonio 5, Texas  
Secretary-Treasurer Lt Col John L Matthews, AAF  
School of Aviation Medicine, Randolph Field, Texas  
Place San Antonio, Brooke General Hospital, Ran-  
dolph Field or San Antonio Aviation Cadet Center  
Time 7 p m, second Tuesday of each month from  
October to May

SAN FRANCISCO COUNTY MEDICAL SOCIETY,  
SECTION ON EYE, EAR, NOSE AND THROAT

Chairman Dr Roy H Parkinson, 870 Market St,  
San Francisco  
Secretary Dr A G Rawlins, 384 Post St, San  
Francisco  
Place Society's Bldg, 2180 Washington St, San Fran-  
cisco Time Fourth Tuesday of every month except  
June, July and December

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THROAT SOCIETY

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Shreveport, La  
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Bldg, Shreveport, La  
Place Shreveport Charity Hospital Time 7 30 p m,  
first Monday of every month except July, August  
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Place Medical Society of District of Columbia Bldg,  
1718 M St N W, Washington, D C Time 7 30  
p m, first Monday in November, January, March  
and May

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

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St, Wilkes-Barre, Pa  
Place Office of chairman Time Last Tuesday of  
each month from October to May

## THE LABILITY OF OCULAR TENSION

### A TEST TO DETERMINE INDIVIDUAL VARIATIONS

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It has long been appreciated that the maintenance of the ocular tension within a relatively narrow physiologic range is a fundamental necessity for the optimal function of the eye. A deviation of pressure below this norm is followed by morphologic changes in ocular structures that interfere grossly with optic performance. An elevation is attended with progressive pathologic alterations in ocular tissues associated with the syndrome complex of glaucoma.

Basically, the pressure within the globe is determined by the opposing forces of the semirigid wall of the eye and the encompassed structures—solid, semisolid and liquid. It is apparent that while the scleral coat and formed contents of the eye normally remain relatively constant, the circulating intraocular fluids—aqueous, blood and perivascular lymph—are potentially subject to changes in volume that establish them as basic determinants of intraocular pressure levels. Since the amount of lymph present in the eye is small, its effect on tension may be ignored in this discussion.

The volume of aqueous within the globe fundamentally depends on the ratio of its speed of formation and outflow. The precise nature of these processes has been disputed, and no one of the many mechanisms that have been suggested, such as transudation, vitalistic secretion, dialyzation or electro-dynamics, has proved completely acceptable. Recently there has been increasing concurrence in the opinion expressed by Friedenwald,<sup>1</sup> that the formation and drainage of the aqueous probably involve many such complex physico-chemical processes in dynamic equilibrium. It is apparent moreover, that in all theories concerning the origin of the aqueous the basic influence of intraocular vascular dynamics must be recognized.

From the Ophthalmological Service of the Mount Sinai Hospital.

Read at a meeting of the New York Academy of Medicine, Section on Ophthalmology, Dec 18, 1944.

<sup>1</sup> Friedenwald, J., cited by Sugar, S. H. Evidence for Circulation of Aqueous and Its Relation to Glaucoma, *Arch Ophth* 28 315 (Aug) 1942.

The volume of blood within the eye, as elsewhere in the body, is undoubtedly under the influence of the autonomic nervous system and the interrelated endocrine glands. In addition, intrinsic ocular reflexes may affect the uveal circulation through antidromic impulses along sensory and sympathetic nerves, possibly through the mediation of the uveal perivascular plexuses, the exact function of which is disputed.<sup>2</sup> Chemically vascular tone is affected not only by the circulating hormones but by local tissue metabolites, typified by histamine.<sup>3</sup> When one considers the vascular capacity of the distensible cavernous tissue of the choroid, the potential role of these automatic agencies in determining ocular tension is more easily appreciated. Thus, Ridley<sup>4</sup> stated that whereas the normal human eye contains 211 cu mm of blood, with complete loss of vascular tone, this capacity is increased by 350 cu mm. The significance of such an augmented volume of blood is emphasized by the fact that an increase of only 150 cu mm of blood is sufficient to raise the normal ocular tension to 70 mm of mercury.

It is obvious, therefore, that the intraocular pressure at any time is dependent on a number of physiologic processes of various degrees of independence. It seems inescapable that their integration and regulation is necessary to maintain the pressure of the globe within a rather narrow normal range. Cannon<sup>5</sup> suggested the term homeostasis to designate those steady states which require complex, coordinated physiologic reactions for their maintenance. He<sup>6</sup> pointed out that in a system composed of unstable structures and subject continuously to disturbance, constancy is in itself evidence that agencies are active or are ready to act to maintain this con-

<sup>2</sup> Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1941, vol 1, p 417.

<sup>3</sup> Duke-Elder,<sup>2</sup> p 420.

<sup>4</sup> Ridley, F., in Ridley, F., and Sorsby, A. *Modern Trends in Ophthalmology*, London, Butterworth & Co., Ltd., 1940, p 361.

<sup>5</sup> Cannon, W. B., in Piersol, G. M. *Cyclopedia of Medicine, Surgery and Specialties*, Philadelphia, F. A. Davis Company, 1939, vol 7, p 306.

<sup>6</sup> Cannon, W. B., in "A. Charles Richet," Paris, 1926, p 91.

stancy It seems reasonable to consider the maintenance of intraocular pressure as a homeostatic system subject to automatic regulatory control for the preservation of the eye at a physiologic optimum

Elwyn<sup>7</sup> ably indicated the apparent inadequacy of local physical processes for the maintenance of intraocular pressure within a fixed normal range He suggested that the normal pressure was a phylogenetically evolved optimum the maintenance of which was regulated by some central autonomic agency similar to the mechanisms controlling such vegetative constants as body temperature and blood pressure As a corollary to this concept, it was suggested that chronic simple glaucoma might be due to an aberration in such regulatory control that manifests itself in elevated intraocular pressure The local morbid anatomic features classically identified with glaucoma are simply the consequences of this etiologically basic regulatory dysfunction It is interesting in this connection to note Cannon's<sup>8</sup> observation that while homeostatic levels are not themselves altered appreciably by advancing age, the effectiveness of the physiologic mechanisms that act to preserve stability is reduced The tendency for essential glaucoma to occur almost exclusively in the older age groups similarly suggests a weakened regulatory control of intraocular pressure with increasing age, though the possible role in the pathogenesis of glaucoma of such local structural changes incidental to aging as enlargement of the lens, sclerosis of the vessels and narrowing of the trabecular spaces also deserves consideration

If such a regulatory mechanism is active, the development of clinically appreciable ocular hypertension may well be preceded by a more or less gradually increasing instability of intraocular pressure In other words, an abnormally increased lability of ocular tension should be manifest as the earliest evidence of deficient regulatory control and incipient glaucoma Pisarello, Kollner, Hagen and others have pointed out the greater variations in the diurnal levels of ocular tension that occur in glaucoma, as compared with the normal curve first described by Maslenikow<sup>9</sup> This spontaneous evidence of increased lability of tension in the eye remains one of the more reliable signs of early chronic simple glaucoma

The idea of a test to indicate the increased lability of a homeostatic system as the earliest

sign of morbid dysfunction is not new In cases of diabetes mellitus and of vascular hypertension, for example, evidence of an increased lability in the regulation of levels of the blood sugar and the blood pressure, as indicated by the dextrose tolerance and the cold pressor test respectively, is considered a valuable indication of impending morbidity The basic idea in such tests is to throw a sudden strain on the homeostatic system by means of a standardized stimulus and to record quantitatively the degree of deviation that occurs and the time necessary for the restoration of the physiologic norm

The value of such a test for detecting glaucoma in its incipency is apparent, since the diagnosis is otherwise made largely through evidence of irreversible ocular damage, which might have been prevented with earlier therapy Appreciation of this fact is indicated by the large number of so-called provocative tests for glaucoma that have been described,<sup>10</sup> quantitatively testifying both to the need for earlier diagnosis of the disease and to the general dissatisfaction, thus far, with the measures devised for that purpose Most of these procedures have aimed at producing abnormal elevations in the pressure of glaucomatous eyes by augmenting the intraglobal volume either by increasing the quantity of fluid entering the eye or by interfering with the drainage of blood or aqueous To our knowledge, no such test has proved definitely diagnostic, since the elevations in intraocular pressure produced have been too small or too inconsistently elicited to be of value

To test effectually the stability of the pressure within the globe requires a stimulus which, when applied to the patient, results in an elevation in ocular tension that is appreciable and is consistently evoked Since, as previously indicated, the global pressure is largely influenced by the volume of intraocular fluids, the production of a sudden increase in the latter should answer this purpose Inasmuch as the formation of aqueous and the degree of engorgement of the uveal bed probably are both dependent on intraocular capillary pressure, an increase in the latter produced by interference with the normal vascular circulation in the eye should augment appreciably the amount of fluid within the globe An increase in inflow of blood and a diminution in drainage had been separately induced by many investigators in various ingenious ways but without the production of consistently satisfactory elevations of ocular pressure It seemed of interest to us, therefore, to explore the possibility of producing

7 Elwyn, H Pathogenesis of Chronic Simple Glaucoma New Concept of Maintenance of Normal Intraocular Pressure, *Arch Ophth* **19** 986 (June) 1938

8 Cannon, W B, in Cowdry, E V Problems of Aging, Baltimore, Williams & Wilkins Company, 1939, p 624

9 Duke-Elder,<sup>2</sup> vol 3, p 3376

10 (a) Duke-Elder,<sup>2</sup> vol 3, p 3389 (b) Gradle, H S *Am J Ophth* **14** 936, 1931, (c) in Ridley, F, and Sorsby, A Modern Trends in Ophthalmology, London, Butterworth & Co, Ltd, 1940, p 200

consistent and appreciable elevations in ocular tension by augmenting the inflow and decreasing the outflow of the vascular supply to the eye simultaneously

#### CONTROL STUDIES

In our preliminary control experiments, the subjects were patients of the ophthalmologic clinic and ward service of the Mount Sinai Hospital. The patient was placed comfortably supine on the examining table, and 1 drop of 0.5 per cent tetracaine hydrochloride was instilled in each eye. A sphygmomanometer cuff was applied to one arm and the patient permitted to rest quietly for a short time to insure basal levels of vascular and intraocular pressures. An object for ocular fixation was selected directly above the patient's head to secure a fixed position of the eyes for tonometric readings. Readings of the ocular tension were taken simultaneously with recordings of the blood pressure. This was done at two minute intervals, a few times, before any stimulus was applied to the patient to establish the normal levels. Immediately after the application of the stimulus, readings were taken every minute for three minutes, then every two minutes for twenty minutes and then every five minutes for about a half-hour thereafter. Curves were drawn to record the exact variations in ocular and vascular pressures that occurred during the period of the experiment, before and after the application of the various stimuli that were tested. In this way, the degree of elevations in pressure produced and the time required for the restitution of the original physiologic levels could be quantitatively appreciated and an impression obtained of the lability of ocular tension and its relation to incidental variations in arterial pressure. Such curves are illustrated in figures 1, 2 and 3.

Although this procedure may seem formidable, it is in practice rather simple and quite safe. In over 180 eyes so tested, the only complaint was that of slight corneal abrasions, which occurred in 4 instances and which healed completely within twenty-four hours with a simple pressure dressing. More frequent abrasions were avoided by the careful observation of certain simple precautions that were evolved in the course of the investigation. The amount of tetracaine hydrochloride instilled into the eye was held at a minimum, i. e., about 1 drop of a 0.5 per cent solution every twenty minutes, since excessive use of the anesthetic seemed to cause a slight edema of the corneal epithelium that increased its susceptibility to abrasion. The patient was instructed to gaze fixedly at the chosen point of observation and carefully to avoid ocular movement during the application of the tonometer. Between recordings, blinking was permitted and was encouraged to avoid excessive drying of the conjunctiva and cornea. As far as possible, readings were made with a single application of the tonometer to the eye, in the proper axis to avoid manipulation on the cornea. A quick second reading was occasionally taken to check an uncertain result. During the experiment the integrity of the corneal surface was constantly observed by means of the reflected image of a light source, and fluorescein was occasionally instilled if a defect was suspected. At the first sign of an erosion further experimentation on that eye was stopped.

While any experimental method that utilizes tonometric results is subject to the inaccuracies of that instrument, with proper technic readings so obtained are well within the margin of error of most clinical methods.<sup>11</sup> Furthermore, by

using as large a series of cases as possible for statistical evaluation, minor instrumental inaccuracies are rendered less significant. This consideration is necessary since tonometry is the only method available clinically for the measurement of variations in intraocular pressure. Schoenberg<sup>12</sup> pointed out several considerations in the proper use of the instrument that were followed in our experiments. With practice it was found that a single application of the tonometer gave a result that was usually reproducible to one half of a division on the Schiøtz scale in a repeated reading.

Since the repeated application to the eye of a weighted instrument, such as the tonometer, induces a gradual decrease of intraocular pressure due to the massaging effect so induced,<sup>13</sup> a series of control experiments were carried out in which tension curves were drawn by the method described, without the application of any test stimulus to the patient. Thirty-two eyes in 20 patients were so treated. The series consisted of 13 normal eyes, 3 aphakic eyes, 1 eye with secondary glaucoma, 2 eyes with chronic simple glaucoma not operated on, 8 eyes that had undergone various filtering operations for primary glaucoma and 5 eyes with various types of cataract. Abnormally high ocular tensions were present in the eye with secondary glaucoma and in 3 eyes with chronic simple glaucoma, 2 of which were under postoperative observation while the other was untreated. No appreciable difference in the lowering effect on tension of repeated applications of the tonometer was noted with these various conditions except that in eyes with originally lower pressures the decline tended to occur sooner and to somewhat greater degree than in globes with higher pressures. Thus, while the average amount of decrease in tension for the entire series was slightly less than 2 mm of mercury Schiøtz, that in 8 eyes with an initial tonometric reading of less than 14 mm was 3 mm of mercury. These decreases in pressure were gradually progressive, irregular and usually first apparent after eight applications of the tonometer, although the interval varied with different eyes. In only 3 eyes was the depression greater than 3 mm of mercury, namely, 4 mm in 2 eyes and 5 mm in a third eye. All these results apply to the tonometer weighted with the 5.5 mg block, since this is the one most frequently employed. In 8 eyes measured with the tonometer weighted with the 7.5 mg block, the average decline in pressure was slightly over 3 mm of mercury, and this began usually, although variably, after the

12 Schoenberg, M. J. *Am J Ophth* 27:70, 1944

13 Duke-Elder,<sup>2</sup> vol 1, p 499

11 Duke-Elder,<sup>2</sup> vol 1, p 500



fourth application of the tonometer. In 1 eye measured with this weight there occurred a gradual drop in pressure of 4 mm of mercury, and in 2 others, a gradual decrease of 5 mm. When the original intraocular pressure was abnormally high, as occurred in the 4 eyes mentioned, the average absolute decrease in tension was the same as that which occurred in the normal pressure group, but the proportional diminution was accordingly much smaller. It must be noted that these results were obtained with a careful technique of single applications of the tonometer, with readings taken as quickly as possible and with minimal manipulation. No appreciable change in systemic blood pressure was noted during these tests. In view of this rather consistent, gradual and relatively slight depressing effect of repeated tonometric tests, it was felt that the massaging effect did not significantly affect the validity of our plan of investigation.

Several methods for inducing an increased flow of blood into the eye were considered. The use of amyl nitrite to induce vasodilation of ocular arterioles was thought inadvisable because of its incidental effects and the difficulty of its administration in uniform dosage. The direct influence of sudden elevations of arterial pressure on intraocular pressure has been clinically observed repeatedly<sup>14</sup> and can be demonstrated experimentally in animals by simultaneous recordings of variations in systemic blood pressure and ocular tension.<sup>15</sup> Sudden increases in global tension immediately consequent to rises in arterial pressure speak for elevated intraocular capillary pressure due to augmented vascular inflow. It may therefore be inferred that, subject to modification by autonomic nervous and hormonal influences and local physicochemical processes, the blood flow to the eye, as to other structures, is directly influenced by the arterial blood pressure. The effect on ocular tension of sudden increases in systemic pressure is recordable because the compensating actions of those agencies that regulate vascular tone do not immediately neutralize the effects of heightened pressure. Methods to increase the blood flow to the eye by transient increases in systemic blood pressure were therefore explored.

Although the blood pressure can be elevated by many drugs, such as pituitary extract, epinephrine and various other sympathomimetics, these were not employed because of such incidental pharmacologic effects as local vasocon-

striction, which might have interfered with the physiologic responses to increased intraocular pressure which we wished to study. Elevations in blood pressure that might be produced by exercise, such as repeated elevation of the legs or by pain induced with the prick of a needle were found to be too inconsistent to be of value for our purpose.

In 1933, Hines and Brown<sup>16</sup> described the so-called cold pressor test, whereby sudden transient elevations in blood pressure were produced, the degree apparently being dependent on the lability of the vascular regulatory processes. These investigators stated the belief that the vasopressor reaction was probably of neurogenic origin and that its speed and the fact that it occurred in adrenalectomized dogs indicated that the production of epinephrine was not concerned in the response evoked. In tests performed on over 500 patients of all types, elevations in blood pressure occurred in 99 per cent of the subjects, with mean elevations in normal persons of 11.4 mm of mercury in systolic pressure and 10.6 mm of mercury in diastolic pressure. In patients with severe hypertension these increases were 47.2 and 34.3 mm respectively. Intermediate groups demonstrated labilities of pressure between these two extremes. Peak elevations occurred between one-half to one minute after the cold application and the pressure usually returned to the original level in about two minutes. In no instance was any seriously adverse side effect noted.

It seemed to us that this method of inducing sudden increases in blood pressure might be used to augment transiently the blood flow to the eye, and so to increase ocular tension. The technique employed for the cold pressor test was similar to that described by its originators.<sup>16b</sup> With the patient prepared, and with blood pressure and tonometric readings taken as described, one of the subject's hands was immersed over the wrist in water at a temperature of 4 C for one minute. The blood pressure and the ocular tension were measured after one minute and then at the intervals previously outlined. Since the vasopressor effect of cold is transient, readings were necessarily quick and prompt. For expediency, blood pressure recordings were usually made immediately after, and not exactly simultaneously with, the measurement of intraocular pressure, and so the correlation between the two, as observed, was not exact.

It was not our purpose to study intensively the effect of the cold pressor test on systemic

14 Cordes, F. C. Early Simple Glaucoma. Its Diagnosis and Management, *Arch Ophth* **17** 896 (May) 1937.

15 Duke-Elder,<sup>2</sup> vol 1, p 512.

16 Hines, E. A., Jr., and Brown, G. E. (a) *Ann Int Med* **7** 209, 1933, (b) *Am Heart J* **11** 1, 1936.



blood pressure and ocular tension, rather, we wished to explore its acceptability as a means of increasing the ocular blood volume and so of influencing the pressure within the globe. For the purpose of our investigation, it was necessary to determine whether or not the effect of the cold pressor test on arterial pressure was consistent and comparable in patients with and without glaucoma. It was also necessary to know whether an increase in blood supply to the eye so induced, and reflected in changes in intraocular pressure, was affected by such individually variable factors as systemic hypertension and the associated instability of regulation of arterial pressure.

Of 32 patients without glaucoma, appreciable increases in blood pressure in response to the cold pressor test were recorded in 30, with an average rise of 21 mm of mercury in systolic pressure and of 11 mm of mercury in diastolic pressure. The range of increases was from 8 to 60 mm in systolic pressure and from 2 to 30 mm in diastolic pressure. According to the standard suggested by Fishberg,<sup>17</sup> 5 of these patients might be considered hypertensive, and in this small group, all of whom showed an elevation in blood pressure, the average increase was 32 mm systolic and 13 mm diastolic. The greater lability of blood pressure in these patients is in accordance with the observations of Hines and Brown.<sup>102</sup>

Of 24 patients with chronic simple glaucoma, an increase in blood pressure in response to this test was recorded in 22, with an average rise of 22 mm of mercury in systolic pressure and of 11 mm of mercury in diastolic pressure. The range of increases in systolic pressure was from 2 to 60 mm and in diastolic pressure from 2 to 26 mm of mercury. Of these 24 glaucomatous patients, there were 8 with clinical vascular hypertension. In these 8 patients there was again noted a more conspicuous elevation of systolic and diastolic pressure in the cold pressor test than occurred in the glaucomatous patients with normal blood pressures, an observation similar to that made concerning the hypertensive patients of the control series.

While the number of patients so tested is too small for definitive conclusions to be drawn, it is striking that the sudden transient elevations in arterial pressure induced with the test occurred with some consistency, were of appreciable magnitude and were essentially similar in normal and in glaucomatous patients.

<sup>17</sup> Fishberg, A. M. Hypertension and Nephritis, ed. 4, Philadelphia, Lea & Febiger, 1939, p. 213.

The simultaneous effect of the cold pressor test on blood pressure and on ocular tension was observed in 28 eyes of 17 patients without glaucoma and in 10 eyes of 7 patients with proved chronic simple glaucoma. The latter group at the time of this examination were receiving no medication and did not have an ocular tension of over 30 mm of mercury Schiötz. It was considered desirable, for purposes of comparison, to consider only those eyes with glaucoma in which tension was within normal limits at the time of examination, though abnormal levels had at previous times been recorded in every case. This was advisable since with elevated tensions the decreased elasticity of the sclera due to stretching tends to cause much greater increases in intraocular pressure per volumetric increase in global content than occur at normal pressure levels.

It was found that an elevation in ocular tension during the cold pressor test occurred fairly

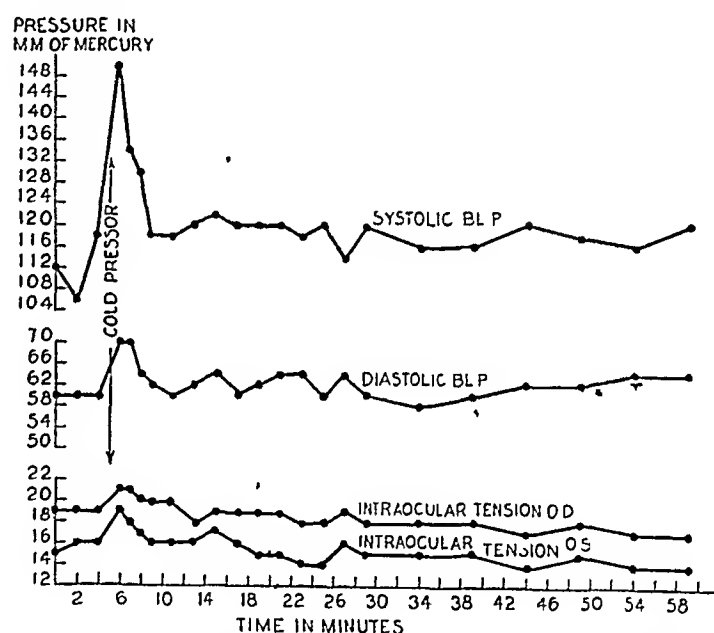


Fig. 1—Typical curves of variations in blood pressure and ocular tension resulting from application of the cold pressor test to a patient without glaucoma.

consistently but was so small that it often fell below the limits of accuracy of our measuring instrument. Thus, of the 28 normal control eyes, 24 showed an increase in global pressure ranging from 1 to 4 mm of mercury Schiötz, with a mean elevation of 2 mm. Figure 1 illustrates the typical response in tension of a normal eye to the cold pressor test, with simultaneous recording of changes in vascular pressure. Of the 10 glaucomatous eyes with tensions at normal levels, 9 showed increases in pressure, ranging from 1 to 4 mm of mercury, with an average rise of 2 mm. All tension curves returned to approximately the original levels after two minutes, as did the response in blood pressure.

These values are too small to permit any inferences to be drawn in a quantitative comparison

of the two groups. However, the one noteworthy fact disclosed in all these 38 eyes was that the rise in ocular tension was not at all proportional to the elevation in arterial pressure which was observed simultaneously. In other words, the systemic vascular response, which apparently occurred similarly in glaucomatous and in non-glaucomatous patients but which varied in degree in the individual patient, seemed to have a relatively constant effect on the blood flow to the eye and on the ocular tension, which was not appreciably influenced by the individual lability of the blood pressure control, within the limits of our instrumental accuracy.

With the requirement for a means to induce an augmented blood flow to the eye through the elevation of arterial pressure apparently satisfied by the cold pressor test, a method for interfering with the drainage of fluid from the eye was sought. Though the precise mode of drainage of aqueous from the globe is still disputed, its ultimate passage, together with the blood from the interior of the eye into the intracranial and facial venous systems, is unquestioned. Venous drainage is continued principally through the internal and external jugular veins, with a relatively small channel existing via the suboccipital plexus into the vertebral and deep cervical veins.<sup>18</sup> A moderate pressure of 40 to 50 mm of mercury applied around the neck was shown by Schoenberg<sup>19</sup> to interfere with the patency of the jugular veins and thus to embarrass ocular venous drainage. This degree of compression, while apparently adequate to occlude the large veins of the neck,<sup>20</sup> could not, of course, interfere with arterial blood flow because of the much higher pressure present in the arteries.

Wessely,<sup>21</sup> in 1906, and Schulze, in 1901,<sup>21</sup> wrote of the rise in intraocular pressure that followed compression of the neck. Thiel<sup>21</sup> noted the elevating effect on ocular tension of venous engorgement induced by lowering the head for a period. He also resorted to the heroic expedient of constricting the jugular veins by cervical pressure for one to two and a half hours and produced a degree of ocular hypertension which only in glaucomatous eyes persisted through the period of cervical compression. This, he surmised, indicated a deficiency in regulation of pressure in such eyes. Schoenberg<sup>19</sup>

suggested that measurable cervical compression could be secured by applying a sphygmomanometer cuff to the neck and showed that the intraocular pressure rose during the inflation of the cuff. The diagnostic implications of this procedure were recognized, but in the results published no consistent differentiation between glaucomatous and nonglaucomatous eyes on the basis of the reaction to venous obstruction was apparent.

The interference with ocular venous drainage provided by lowering the head seemed too variable a means of raising intraocular tension, and the recording of its effect with the tonometer, in that position, was most inconvenient. On the other hand, the easy applicability and simple standardization possible with cervical compression recommended the latter procedure for our purpose. To study its possibilities, another control series of patients were tested with the following technique.

A sphygmomanometer cuff was applied with comfortable laxness about the patient's neck, and another cuff was applied to his arm. The procedure was explained to the patient to allay his anxiety, and he was permitted to lie quietly supine to assure basal levels of blood pressure and ocular tension. When the pressures had apparently reached equilibrium, the stimulus was applied by inflating the cuff about the patient's neck to 40 to 50 mm of mercury, as recorded on the sphygmomanometer, and maintaining this pressure until after the tonometric reading had been taken. This was done exactly after one minute of cervical compression, simultaneously with a recording of arterial pressure. Readings were then continued after release of the cervical compression, with the patient at rest, at the intervals described. Such transient cervical compression was safely tolerated by all patients tested, without excessive discomfort.

Forty-seven eyes were so studied. Twenty-nine of these were in 17 patients without glaucoma. This number included 12 eyes with cataract, 3 with aphakia and 14 without apparent abnormality. No difference in response of these various groups was noted. Measurable increases in ocular tension occurred in 21 of these 29 eyes, but in 16 they were 3 mm or less of mercury Shiotz so that their magnitude frequently fell below our limit of accurate measurability. The range of elevations varied from 1 to 7 mm of mercury, with an average rise of 3.2 mm. In these, as in all other eyes so tested, the tension returned to the original base line or slightly below within one minute of the release of cervical compression. Figure 2 contains a typical curve of response of the intraocular pressure to cervical compression, with simultaneous recording of variations in blood pressure.

Of these 17 patients without essential glaucoma, 9 showed a measurable increase in arterial pressure during jugular compression, ranging

18 Gray, H. *Anatomy*, edited by T. P. Pick, ed 13, Philadelphia, Lea Bros & Co., 1893, p. 653.

19 Schoenberg, M. J. Remarks on Artificial Induction of Ocular Hypertension by Compression of Jugular Veins, *Arch Ophth* 1: 681 (June) 1929.

20 Starling, E. H. *Principles of Human Physiology*, ed 4, Philadelphia, Lea & Febiger, 1926, p. 808.

21 Cited by Schoenberg.<sup>19</sup>

from 4 to 16 mm of mercury systolic and 2 to 6 mm of mercury diastolic, with average rises of 9 and 4 mm respectively. While these elevations were not high, it was noticeable that there was a qualitative correlation between the occurrence of elevation of systemic blood pressure and the degree of rise of ocular tension during this test. Thus, the average rise in ocular tension in patients with no elevation in arterial pressure was 1.7 mm of mercury Schiötz, as compared with an average rise of 3.4 mm in patients whose systemic blood pressure showed a coincidental elevation. These differences are too small to be conclusive, but they are suggestive of the influence of variations in arterial pressure on responses of global pressure to cervical compression.

Nine eyes, in 6 patients with proved chronic simple glaucoma who, though under no medi-

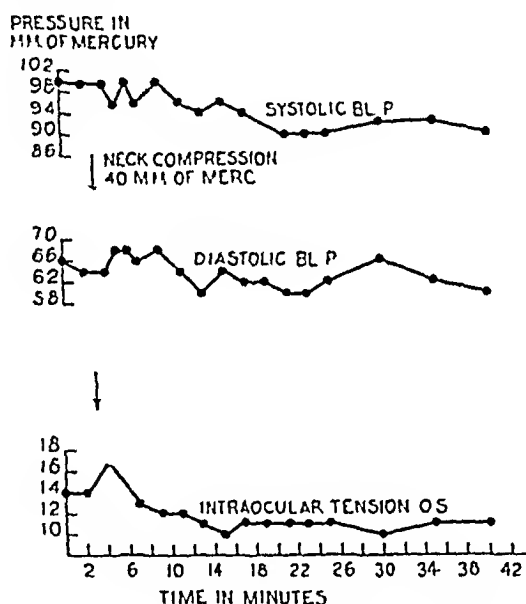


Fig 2—Typical curves of variations in blood pressure and ocular tension when cervical compression of 40 mm of mercury was applied for one minute. In this instance no appreciable rise in blood pressure occurred.

cation at the time of the experiment, had ocular tension of less than 30 mm of mercury, were studied for purposes of comparison. Elevations in ocular tension followed compression of the neck in 8 of these eyes, ranging from 2 to 19 mm of mercury, with an average rise of 7.3 mm. Although this would seem to be significantly higher than the rise in global pressure that occurred in nonglaucomatous eyes, in this series there were several eyes with established glaucoma in which the rise in tension was below the average for the normal group, and a marked overlapping of the range of elevation in the two series of eyes generally precluded the drawing of diagnostic inferences. These results are similar to those published by Schoenberg.<sup>19</sup>

In this glaucomatous group, it was again noted that in 4 of the 6 patients an appreciable rise of

arterial tension occurred during the test, averaging 13 mm. of mercury systolic and 6 mm. of mercury diastolic. Although no quantitative relation between the rise in ocular tension and the rise in blood pressure could be established, it was obvious that in the 4 patients with elevated vascular tension the rise in intraocular pressure was much higher, i. e., an average of 8 mm. of mercury, as compared with an average rise of 1.2 mm. of mercury in the 2 patients with glaucoma in whom no elevation in arterial pressure occurred during the test.

A third group of 9 eyes with chronic simple glaucoma, in 6 patients whose ocular tension without medication was over 30 mm. of mercury, were tested with cervical compression. Here it was found that elevations in tension occurred ranging from 2 to 25 mm. of mercury, with an average rise of 12 mm. Here, again, however, a marked overlap of the range of elevations with that of the normal group was present, and once more the qualitatively greater rise in tension was noted when elevation of arterial pressure occurred.

It seems apparent that while some difference in the response of glaucomatous and that of normal eyes to simple jugular compression exists, no diagnostic value can be attached to the test in individual cases. However, it seems that one factor contributory to variability in intraocular pressure was ignored in these early tests based on cervical constriction, namely, the coincidental psychic effect on systemic blood pressure. It is obvious that even in moderately apprehensive patients an increase in blood pressure might take place during such a procedure which would augment the effect of the cervical compression on ocular tension beyond that which would occur in a more phlegmatic subject with unaltered arterial tension. One may suppose that while the outflow of blood from the eye is impeded with some uniformity by the test, the inflow is not only uncontrolled but excited to individually varying degrees. These inferences are supported by the variations in arterial pressure that occurred during our tests and by the correlations found to exist between such rises in vascular pressure and the degree of response in ocular tension simultaneously noted. It seemed to us, therefore, that by increasing arterial pressure with some consistency and so augmenting the inflow of blood in each case simultaneously with the constriction of jugular vessels, a more comparable elevation in ocular tension would result in all instances. It was thought that this concurrent effect might be secured with some constancy by the simultaneous application of the cold pressor and the

jugular compression test, and a simple method of combining the two was devised

#### METHOD FOR TESTING LABILITY OF OCULAR TENSION

The patient lies supine and is asked to look at an object directly over his head to insure a fixed vertical position of the eyes for tonometric recording. A sphygmomanometer cuff is placed loosely about his neck. After a short period of rest two or three tonometric readings are taken at brief intervals to establish the base line of ocular tension for that patient. One of his hands is then immersed over the wrist in ice water ( $4^{\circ}\text{C}$ ). Simultaneously the cervical cuff is inflated to a pressure of 40 to 50 mm of mercury, as recorded on the attached manometer, and is maintained at that level during the period of the test. The ocular tension is measured quickly and promptly after one minute, and the ice water is then removed and the cuff deflated

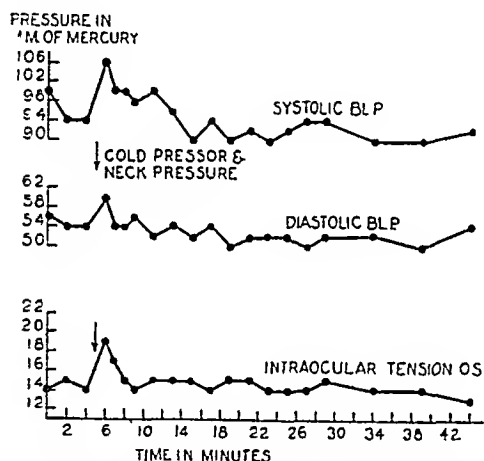


Fig 3—Typical curves of variations in blood pressure and ocular tension when the combined cold pressor test and cervical compression were applied for one minute

Early in our investigation the measurements were taken as previously described over a long period. A typical curve of response in tension to the combined stimuli is illustrated in figure 3. However, we found consistently that in all eyes elevations in tension so induced returned to the level of the original pressure within two minutes after the stimuli were removed, so that no measurable difference could be shown to exist between different eyes in the time required for the reestablishment of the original pressure level. Accordingly the basal ocular tension before application of the stimulus and the tonometric reading immediately thereafter were considered sufficient data for the clinical interpretation of the test.

Furthermore, in a series of 17 normal patients, measurements of blood pressure were taken simultaneously with the recording of ocular tension

during the performance of this test. All showed an elevation of systolic and diastolic pressure similar to that produced by the cold pressor test alone, as previously studied, and once more it was observed that the tension reaction in the eye was not proportional to the vasopressor response shown by the change in arterial pressure. It was therefore felt that in the clinical performance of the test a control record of variation in blood pressure was unnecessary.

A total of 96 eyes in 56 patients were first studied. The average age of the patients without glaucoma was about 48 years, and all but 8 of the subjects were more than 35 years old; this selection was made to insure an age level comparable with that of the group with chronic simple glaucoma. Seventy-seven nonglaucomatous eyes were studied, including many with various degrees of cataract development, some with postoperative aphakia and a majority with no apparent ocular abnormality. There was no consistent difference in response of any of these subgroups of the nonglaucomatous eyes.

Of these 77 eyes, 75 exhibited an increase of ocular tension with this combined stimulus, while 2 showed no change. In 71 eyes the increase ranged from 1 to 9 mm of mercury Schiötz, and in a single eye in 2 patients and in both eyes of another patient the elevations were 12, 10, 17 and 11 mm of mercury respectively. It is regrettable that the opportunity was not afforded to study these 3 patients more extensively in order to check on the nonglaucomatous evaluation of their condition, but it may be noteworthy that 3 of these eyes presented an intumescent cataract and a shallow anterior chamber. An attempt will be made to obtain a follow-up study of these patients to determine the possible presence of a glaucomatous diathesis. The average rise in tension in all the nonglaucomatous eyes tested was 5 mm of mercury.

Nineteen eyes in 14 patients with chronic simple glaucoma, all of which had at some time shown increased tension and for which the diagnosis was unquestioned, were chosen for comparative study. None of these eyes had undergone operation of any type, and at the time of our study they had not been exposed to medical therapy for at least twenty-four hours. These restrictions were thought advisable to avoid any conflicting reactions that might be induced by operative intervention or pharmacologic effects. For purposes of comparison with the normal group, 7 eyes with glaucoma simplex in which the tensions at the time of our study were all below 26 mm of mercury Schiötz were first tested. The elevation in ocular tension produced

in this group ranged from 9 mm of mercury, in 1 eye, to 19 mm of mercury, with an average rise of 13.5 mm. In the other group, of 12 eyes in 8 patients with chronic simple glaucoma, in which the ocular tension at the time of the test was 30 mm of mercury or over and ranged up to 48 mm of mercury, the variation in elevation of global pressure was from 8 to 30 mm of mercury, including a single instance of ocular tension of 8 mm and another of 9 mm of mercury. The average rise of tension in this group was 14.8 mm of mercury. The actual changes in tension that occurred in all eyes tested are graphically recorded and grouped in figure 4.

It is thus indicated that the procedure described is capable of inducing an easily appreciated transient rise in ocular tension with some consistency. Our results in the series of tests made thus far suggest that there is a difference in the degree of elevation which occurs in nonglaucomatous eyes and that which occurs in eyes

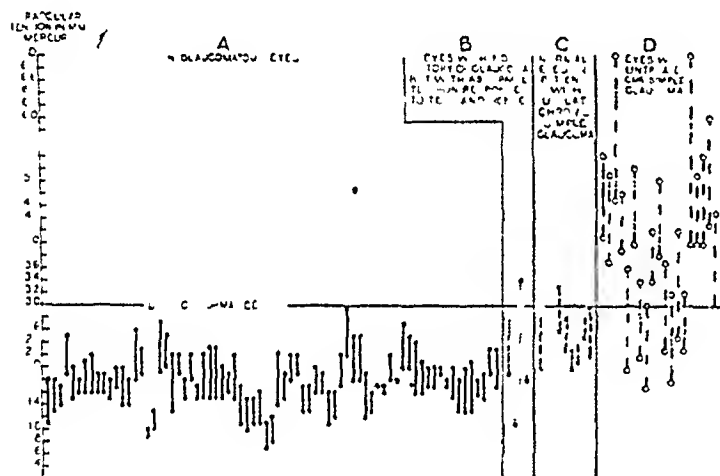


Fig 4—Graphic representation of elevations of tension and ceilings of pressure attained in response to simultaneous application of the cold pressor test and cervical compression in eyes without known glaucoma, in normal eyes of patients with unilateral chronic simple glaucoma and in eyes with chronic simple glaucoma which had received no medical or surgical treatment.

with chronic simple glaucoma, an arbitrary figure of 9 mm of mercury approximately indicating the maximal rise occurring in normal eyes. An elevation above this figure may be considered at least suggestive of morbidity.

In examining the results of these experiments, another interesting observation was made. In addition to noting the degree of elevation in ocular tension that occurred, the absolute height to which the pressure in each eye rose was recorded. In conformance with the terminology applied by Hines and Brown<sup>16b</sup> to variations in arterial pressure, such elevated levels of ocular tension might be referred to as the ceiling of pressure reached in each case.

As shown in figure 4, of the 77 nonglaucomatous eyes studied, this ceiling was over 30 mm

of mercury in only 1, that in which the highest elevation of 17 mm of mercury was recorded, and a level of 34 mm of mercury resulted. Ceilings for the remaining 76 eyes ranged from 15 to 30 mm of mercury, the latter level being reached in only 1 eye. The average height of the pressure ceilings reached in this control group was 20.3 mm of mercury.

In the 7 eyes with chronic simple glaucoma but with initial tensions within the normal range, comparable to those of the nonglaucomatous eyes, the ceilings at the end of the tests ranged from 30 mm of mercury, in 1 instance, to 43 mm of mercury, with the average height in intraocular pressure elevated to 35.4 mm of mercury. In the 12 eyes with chronic simple glaucoma in which the initial pressures had been over 30 mm of mercury, the ceiling levels reached were, of course, in a much higher range, namely, 48 to 74 mm of mercury.

If one accepts 30 mm of mercury as an upper limit for the normal pressure within the eye, as measured with the Schiötz tonometer,<sup>22</sup> it is apparent that in only 1 of 77 nonglaucomatous eyes so tested did the ceiling of ocular tension rise above this level. On the other hand, in every eye with chronic simple glaucoma thus examined this figure was either reached or exceeded. These facts are illustrated graphically in figure 4.

While there is a fairly consistent correlation between the degree of elevation of tension and the height of the ceiling reached, this is not constant. Three eyes without definite glaucoma were noted in which, in spite of an abnormal degree of elevation of pressure with this test, the level of tension reached, though moderately high, was still within normal limits. Conversely, there were 3 eyes with compensated glaucoma in which, because of an initial relatively high level of tension, a maximally normal degree of elevation occurred that sufficed to raise the ceiling to abnormal heights. It seems therefore that while the higher degrees of elevation would tend to raise the level of intraocular pressure during the test to abnormal heights, in the unusual cases in which the original pressures were sufficiently low, this did not occur. Though the increased lability of tension in such cases, indicated by abnormal rises in pressure, may be considered a constant threat of morbidity, its potentially noxious effect may be neutralized by the physiologic low tension level, and such eyes, accordingly, showed no glaucomatous stigmas. When, however, the original pressure was apparently geared to a higher level, even an only slightly high lability of tension, expressed by an elevation of moderate



degree, was sufficient to raise the ceiling to abnormal amounts. Such eyes, in our series, showed clinical evidence of glaucoma. It is suggested, therefore, that while demonstrably abnormal lability of tension might be considered contributory to morbidity, an abnormally high ceiling of tension is even greater evidence of a tendency toward intraocular hypertension. Furthermore, while the value of the rise of tension demonstrated by this test depends on the recording of a truly basal level initially, the validity of the ceiling pressure noted is independent of the actual physiologic level.

It should be noted that, just as Hines and Brown<sup>16b</sup> demonstrated the approximate consistency of the responses to the cold pressor test in any individual subject, the elevation in ocular tension induced by this test remained qualitatively the same with repeated experiments on the same eye. When the test was repeated on 15 eyes in normal subjects and on 15 eyes of persons

blood pressure so produced is shown in figure 5. Our purpose was to investigate the individual contribution of each stimulus to the combined effect on ocular tension. No constant relationship was discernible between the elevating effect on global pressure of either individual stimulus and the response to the combination of the two. It was apparent, moreover, that the combined effect on tension was not a simple quantitative summation of the responses of the individual stimuli. It was further noted that when both eyes in 1 patient without glaucoma were tested, the response of ocular tension to the stimuli applied individually and in combination was qualitatively, but not quantitatively, similar in the two eyes. In patients with bilateral or unilateral glaucoma, the elevations in tension produced in the two eyes by these stimuli seemed unrelated to each other.

#### COMMENT

Although the number of cases here studied is not large, from the data thus derived certain interesting impressions emerge. The simultaneous application to a patient of the cold pressor test and jugular compression fairly consistently results in a measurable increase in ocular tension. The amount of elevation that occurs in response to this easily standardized combined stimulus may be regarded at least as a qualitative expression of the lability of intraocular pressure and is appreciably greater in some eyes than in others. In the small series of cases we studied, the eyes in which lability of tension seemed highest almost uniformly were afflicted with chronic simple glaucoma, a finding conforming to the concept previously discussed, that the disease may be considered due to an aberration in the homeostasis of intraocular pressure. However, since the precise disturbance underlying essential glaucoma is disputed, it is permissible only to say that abnormal lability of tension as demonstrated by this test seems to be present in chronic simple glaucoma and, when found in an eye, may be associated with that disease. We have not yet had the opportunity to study the reaction to this test of a sufficient number of eyes with secondary glaucoma to be able to demonstrate satisfactorily a differentiating reaction in such eyes. We are also studying the response to this test of eyes subject to acute congestive glaucoma.

The precise mechanism whereby the rise in intraocular pressure occurs in response to this combination of stimuli is uncertain. It seems probable that a sudden engorgement of intraocular tissues is produced. In accordance with the mechanism suggested by Gradle<sup>10c</sup> to explain

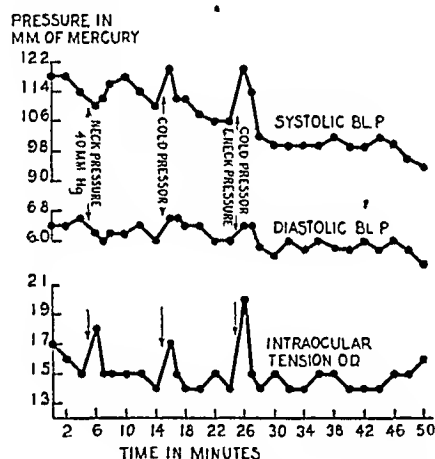


Fig 5—Curves showing variations in blood pressure and ocular tension during application of the cold pressor test and cervical compression separately and then simultaneously to a patient without glaucoma.

with chronic simple glaucoma, though differences in degree of elevation of tension up to 5 mm of mercury were noted, in no instance was the variation great enough to change the result from normal to abnormal or vice versa. The most significant change occurred in an eye with glaucoma in which on repetition the elevation of tension was 7 mm of mercury, as compared with a previous 11 mm and the ceiling of pressure changed to 29 mm of mercury from the earlier 34 mm. The interpretation here necessarily was altered from that of definite to that of suggestive abnormality in the regulation of ocular tension.

More than 50 eyes were tested with the separate application, at sufficient intervals, of the cold pressor test and of cervical compression and then with the two procedures simultaneously. A typical curve of variations in ocular tension and

the rise in tension occurring in many so-called provocative tests, it might be assumed that a swelling of the iris root results that might occlude the angle of the anterior chamber. He stated the belief that this might embarrass drainage of intraocular fluids sufficiently to increase intraocular pressure to a degree depending on the width of the angle and the relative swelling of adjacent tissues. However, the speed with which the increase and decline of pressure occurs here renders such an explanation unlikely. Furthermore, the depth of the anterior chamber as clinically estimated seemed to bear no relation to the degree of ocular response to this test.

If one attributes the rise in tension to the sudden congestion of intraocular tissues caused by the combination of interference with venous drainage and an increase in vascular inflow, another explanation of the variation in response in different eyes readily offers itself. One might assume the presence of a reflex arc coordinating vascular inflow and outflow within the eye for the purpose of preventing excessive intraocular congestion. The application of jugular compression might therefore initiate a marked compensatory vasomotor reaction in the afferent arterioles of the eye, to effect a diminution in inflow of blood. It is obvious that the strain put on such a vasoconstriction by a simultaneous rise in systemic blood pressure that would augment the flow of blood to the eye might overcome this compensatory mechanism in varying degrees in different eyes and result proportionately in congestion and ocular hypertension. It follows that this test may measure the effectiveness of such a protective vasoconstrictive reflex, and an abnormal increase in tension so demonstrated may indicate a breakdown in the arc that may be associated, though not necessarily etiologically, with chronic simple glaucoma.

It has been suggested that the impairment of such vascular coordination may be a precursor to actual glaucoma, and its demonstration might therefore reveal a glaucomatous diathesis. In 6 out of 8 apparently normal eyes of patients with unilateral chronic simple glaucoma, however, normal lability of ocular tension was present. The average rise of tension in these few eyes was 5.8 mm of mercury, and the mean ceiling reached was 26.3 mm of mercury. These figures, though higher than the corresponding averages of 5.0 and 20.3 mm in the control group, cannot be considered definite evidence in favor of such a contention. However, it is suggestive that they tend to fall between the values for the normal and those for the glaucomatous group. The re-

sults of the test on these cases are illustrated in figure 4.

The nature of such a coordination of the ocular vascular system is conjectural. It may be nervous or physicochemical or both, and may be either completely intrinsic to the eye or mediated through extraocular autonomic agencies. In regard to the latter possibility, it may be mentioned that in 1 eye with a complete Horner syndrome the lability of ocular tension thus tested was well within normal limits.

The effect of various drugs on the response to this test is now being studied. These investigations are not yet completed, but it may be mentioned at this time that pilocarpine in clinical dosage appreciably reduced the abnormal lability of tension, as demonstrated by this test, in each of 13 eyes with chronic simple glaucoma which had not been operated on. The elevations in tension produced by this combined stimulus

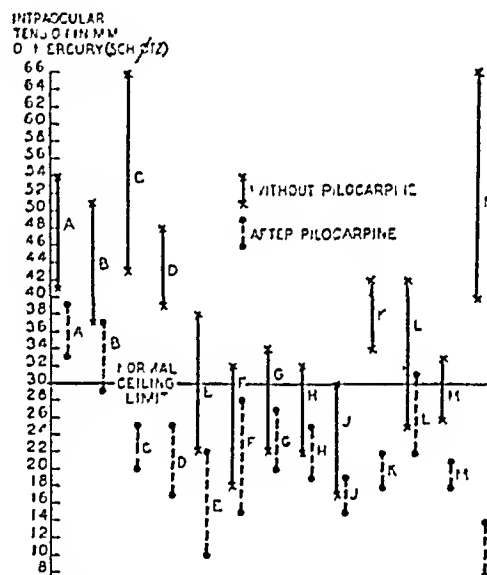


Fig 6—Graphic representation of elevation of tension and ceiling of pressure reached in eyes with chronic simple glaucoma which had not been operated on after simultaneous application of the cold pressor test and cervical compression, before and after instillation of pilocarpine. Each eye is denoted by an individual letter.

before and after the instillation of pilocarpine in these eyes are illustrated in figure 6. Furthermore, it was indicated in these eyes that only when the glaucomatous hypertension was clinically controlled successfully with pilocarpine was the abnormal lability and ceiling previously demonstrated in the absence of the drug reduced to normal range after pilocarpine had been instilled. Such a stabilizing effect of pilocarpine on the lability of intraocular pressure was less certain in normal eyes, occurring in 11 out of 17 nonglaucomatous eyes, and to a degree usually so small that it fell below our range of accurate measurement. There is some evidence based on such experiments on a glaucomatous eye with fixed pupil that this action of pilocarpine on



the abnormal lability of tension in glaucoma is independent of its miotic effect. The implication is apparent that pilocarpine and pharmacologically related drugs may play a role in the reflex arc previously mentioned as a possible coordinating mechanism between vascular inflow and outflow in the eye.

It may also be noted that in a small group of 7 eyes with chronic simple glaucoma which had undergone various filtering operations and in which no further therapy was required to control the pressure, the response to this test was normal in elevation and ceiling of tension in all instances. Conversely, abnormal rises of tension occurred in 4 out of 5 eyes with chronic simple glaucoma tested without medication when operation in itself had proved ineffectual in reducing tension to normal levels. These preliminary impressions are mentioned to suggest the possible value of this test in quickly estimating the therapeutic efficacy of pharmacologic or operative measures in any case of chronic simple glaucoma.

#### CONCLUSIONS

1 The normal maintenance of intraocular pressure within an optimum range suggests the presence of a regulatory mechanism.

2 Dysfunction of such a homeostatic system may result in abnormal lability of intraocular pressure and may eventuate in chronic simple glaucoma.

3 The method here described to test this lability may prove of value for the earlier diagnosis of chronic simple glaucoma and the evaluation of therapeutic measures for that disease.

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#### DISCUSSION

DR WILLIS S. KNIGHTON, New York. Dr Lambert and Dr Bloomfield are to be congratulated on their excellent presentation, and especially on the restraint which they have exercised in interpreting their results.

They have ingeniously combined two well known provocative tests for glaucoma so that the amount of induced vascular congestion is standard for each patient and can be reproduced at any time.

The results of other provocative tests in use at the present time are so uncertain that one does not dare deny the existence of glaucoma when the result is negative. But if the lability of intraocular pressure, as presented here, is an accurate indication of the glaucomatous status, it may yet be possible to prove the absence of glaucoma.

The only practical way to prove the validity of a test is to try it, and I have subjected 12 patients

to this procedure. I should like to refer briefly to the results with some of them, as a sample.

The first 2 patients showed no evidence of glaucoma. One of them had nuclear cataracts. In neither patient was the variation of tension more than 4 mm of mercury and the highest ceiling was 25 mm of mercury. This is what one would expect in the absence of glaucoma.

Patient 3 had early glaucoma simplex. His ocular tension had never been over 35 mm of mercury with other provocative tests, but there were early changes in the fields and his eyes were uncomfortable without the use of drops. The visual acuity, visual fields and ocular tension have been controlled for three years with weak solutions of pilocarpine, but when the dose has been reduced or the drops omitted, the tension has slowly risen above 30 mm of mercury in one eye or the other. The drops were omitted for one week prior to this test, with the result shown. The tension in the right eye rose to 35 mm of mercury, after an excursion of 8 mm, but the tension in the left eye dropped 2 mm. It is interesting to note that the highest point in the tension in the right eye reached with this test did not exceed the maximum obtained with other provocative tests and no new information was added. I cannot explain the reaction of the left eye except to say that on previous occasions the eyes seemed to alternate in their manifestation of subjective symptoms and in the elevation of the tension. The paracentral fields were equally defective, and it would be difficult to say clinically which eye was the worse except for the occasional differences in tension. Perhaps some local control mechanism was in force at the time of this test, but if one were to rely on this single examination, one would be forced to the erroneous conclusion that the left eye was normal. A single test, obviously, is not conclusive.

Patient 4 had had an iridencleisis on the right eye after an acute attack of glaucoma. The tension remained at about 22 mm of mercury without medication. The tension of the intact, left eye seemed to be controlled with use of pilocarpine at night only. The pressor-congestion test indicated that the tension of the right eye was under control. It is interesting to note that the lability, as well as the level of the tension, was normal. It can hardly be argued that a simple paracentesis would have accomplished the same result by changing the characteristics of the aqueous, for this test was made about one month after the operation. Kronfeld has shown that the aqueous returns to its primary composition about two weeks after paracentesis. The tension of the intact, or left, eye rose to a suspicious height. Although pilocarpine was being used at night, the last drop had been administered fifteen or sixteen hours before the test, and the medication was probably insufficient.

Patient 5 showed the reaction of the tension after trephination of each eye. Again, the

lability, as well as the height, of the tension was normal

Patient 6 had glaucoma six years ago, the tension of the right eye was 40 mm of mercury, and there was a paracentral wing scotoma in each eye. Pilocarpine had been used for a short time and then discontinued. The patient has been without drops for six years, and clinically his glaucoma is no worse. The lability and height of tension are apparently normal. If these factors are an indication of the state of his glaucoma, he is not in danger.

Dr. Givner told me of another patient who showed a lability of tension of 17 mm of mercury in the right eye and of 13 mm in the left eye. The ceilings were 40 and 36 mm respectively. Other provocative tests had failed to raise the tension to an amount which would incite suspicion. The clinical findings, however, included deep cupping and paracentral scotomas, so glaucoma was already evident. The test for lability merely indicated the degree of abnormality.

Excessive lability of the intraocular pressure is undoubtedly one of the earliest manifestations of essential glaucoma. Elevated tension must be present at some time in every case of true glaucoma. Even when glaucoma cannot be demonstrated, the only other changes that occur in the eye are those which have been proved to be secondary.

In other patients who had glaucoma without increased tension the disease was found to be secondary to calcification of the cerebral and ophthalmic arteries and was not true glaucoma.

I cannot agree with persons who say that primary glaucoma is caused by secondary changes in the eyes resulting from age, although such changes may be factors in modifying a pressure that is already aberrant. But the abnormal pressure comes first.

There must be a controlling mechanism to hold the normal pressure within such narrow confines, but its nature and location will have to await further investigation. It is difficult to visualize a central mechanism, such as Elwyn proposed, that would permit the disease in one eye to progress so much farther than that in the fellow eye. On the other hand, Friedenwald's conception of local ocular control fails to explain many things. The authors have postulated a reflex arc, location unknown, while admitting the possible influence of local factors coincident with age.

Regardless of the site of this control, it remains to be seen whether this pressure-congestion test will show an early lability of tension in advance of the present diagnostic methods. There is some indication that it may do so in cases of so-called unilateral simple glaucoma. I question the possibility that such a condition could exist, although Duke-Elder speaks of the other, "healthy," eye in cases of glaucoma. Other authors maintain that the second eye is not

healthy but that undiscovered, preclinical glaucoma exists. The authors themselves found that the supposedly unaffected eyes showed lability of a degree that fell between that of the normal and that of the glaucomatous group. The interesting point is the suggestion that the second eye was not quite normal in its reaction. Perhaps a repetition of the test will give more positive information. The response in my own patient with chronic simple glaucoma demonstrated the fallibility of a single test.

Early glaucoma will never be easy to discover, and this test can do no more than indicate a variable in one of its phases. The lability of the tension will never be great in cases of questionable early glaucoma because, as is indicated by the low ceiling of tension, which makes the diagnosis difficult, fairly active compensatory factors are at work. Not the least of these is the elasticity of the corneoscleral coat, which takes up some of the increased pressure without transmitting it to the tonometer. As this elasticity diminishes, less intraocular pressure can be absorbed, and any increase in the volumetric content of the globe is more evident. But, at the same time, the ceiling tension is elevated, and the diagnosis is more apparent. The greatest help is needed in cases of early glaucoma with low tension.

As the authors have indicated, many interesting questions suggest themselves, such as the effects of various drugs and the reactions in cases of so-called secondary glaucoma.

In the meantime, this test is a practical, informative one, which will undoubtedly prove more valuable as it is better understood.

DR. HERMAN ELWYN, New York. The work of Dr. Lambert and Dr. Bloomfield is a valuable addition to the knowledge of glaucoma, whether the lability test turns out to be practical or not. The lability of the intraocular pressure which is characteristic of the early stages of chronic simple glaucoma can be measured with their test. The test also shows that this lability can be brought to normal with the use of pilocarpine. This is important, for it leads to certain theoretic deductions as to the pathogenesis of glaucoma.

Pilocarpine is a cholinergic drug, and it is known to act on the effector cells innervated by cholinergic nerve fibers. It is known that the normal intraocular pressure is maintained by cholinergic nerve fibers which act through the mediation of acetylcholine. This is demonstrated by the known action of physostigmine in preventing the destruction of acetylcholine by cholinesterase. Thus, in cases of increased intraocular pressure use of physostigmine permits acetylcholine to act on the effector organ and the intraocular pressure is reduced. The action of pilocarpine, which is the same as that of acetylcholine in normalizing the labile intraocular pressure of early glaucoma, seems to me to prove that the effector organ for the maintenance of the intraocular pressure is intact.

In early glaucoma, then, the effector organ is intact, and the chemical mediator is produced and reaches the effector organ at times, that is, when the intraocular pressure is normal. When the pressure is increased, acetylcholine can be made to reach the effector organ by preventing its destruction by means of physostigmine. Obviously, however, the chemical mediator is produced in uneven amounts—sometimes in amounts sufficient to maintain the normal pressure, at other times in insufficient amounts. Regulation of its production is at fault. But where is this fault located?

Acetylcholine is produced at the terminal nerve endings of the cholinergic postganglionic nerve fibers. Their production is not regulated there, for the impulse to production comes from the nerve cells, which are located in the ciliary ganglion. This ganglion, like all peripheral ganglia from which postganglionic nerve fibers arise, is not a regulatory center, but a distributive one for impulses coming from preganglionic fibers. Preganglionic fibers to the ciliary ganglion come from the small cells of the nucleus of the third nerve. Impulses for the continued uniform production of the chemical mediator at the nerve endings in the eye must be regulated from these cells, or from other centers in the brain which send impulses to these cells.

With the effector organ in normal condition in the early stages of glaucoma, as shown by the effect of pilocarpine in normalizing the labile intraocular pressure, the irregularity in the production of the chemical mediator can be due only to irregular impulses coming from the cells of the preganglionic nerve fibers, that is, from the centers in the brain. The work of Lambert and Bloomfield gives added evidence in support of the assumption that the primary fault in glaucoma is a disturbance in the regulatory center in the brain the function of which it is to maintain the normal intraocular pressure.

DR LUDWIG VON SALLMANN, New York. I have had no experience with the new lability test, but many years ago I studied the two tests on which it is based. Kahler and I observed in normal human subjects the tendency to an inverse response of the blood pressure and the ocular pressure to thermal stimuli, that is, as the blood pressure increased with a cold stimulus, the intraocular pressure decreased slightly. These observations are at variance with the results in the present study. The statement of Dr. Bloomfield in regard to the unreliability of the jugular compression test is in agreement with general experience. It seems possible that the combina-

tion of two unsatisfactory tests may result in a useful diagnostic procedure. But would it not be more feasible to combine the jugular compression test with the heat stimulus test, since the latter sometimes produces a slight rise in the intraocular pressure?

DR SYLVAN BLOOMFIELD, New York. I wish to thank the discussers for their constructive comments.

We did not observe in our series a response like that which occurred in the patient in Dr. Knighton's series whose ocular tension fell on application of the stimuli. It is difficult for me to understand how the congestion induced in an eye with this test could result in a drop in intraocular pressure. I should be interested in a repetition of the test on that patient. I am also interested in his patient who had an episode of glaucoma which was followed by normal tension without treatment and who now, six years later, gives a normal response to our test. The only parallel I can think of occurred in 2 patients with acute congestive glaucoma, who showed increased lability of ocular tension with this test during the acute episode and who, after medical control of the attack, gave a normal response a month or two later, when the disease was in a quiescent phase. I suggest the possibility that Dr. Knighton's patient had an episode of acute congestive glaucoma, rather than chronic simple glaucoma.

In answer to Dr. von Sallmann's question, I can only say that in almost all of a series of about 40 eyes on which we tried the cold pressor test alone, a definite, though small, increase in tension occurred, and this experience seems to agree with that of investigators who produce elevations in blood pressure by other means. There seems to be evidence that an increase in blood pressure often is associated with a transient rise in intraocular pressure.

I know nothing about the use of hot water for this purpose. It sounds interesting, and we may try it next.

DR ROBERT K. LAMBERT, New York. I think I can confirm Dr. von Sallmann's findings in one respect. In preliminary experiments at Montefiore Hospital, we studied the effect of elevating the blood pressure on the intraocular tension in normal persons. There must be an active compensatory mechanism at work, for the systemic injection of epinephrine and solution of posterior pituitary not infrequently produced a slight lowering of intraocular tension, after an initial slight rise. I do not believe this mechanism is as active in cases of glaucoma or of preglaucoma.

# GONORRHEAL SYNDROME WITHOUT GONORRHEA

## REITER'S DISEASE

LIEUTENANT COLONEL ROBERT L. LUCAS AND MAJOR HARRY WEISS

MEDICAL CORPS, ARMY OF THE UNITED STATES

The association of urethritis conjunctivitis and arthritis and cutaneous lesions is a syndrome not uncommonly produced by the gonococcus

Forty-seven cases<sup>1</sup> in which the gonococcus could not be found in relationship to this syndrome have been reported in the literature since 1912. The most recent article on this subject was one by Lever and Crawford,<sup>1</sup> who reviewed the subject from its dermatologic aspects.

The triad of urethritis, conjunctivitis and arthritis occurring in this order, in the absence of a gonococcal etiology, has come to be known as Reiter's disease.<sup>2</sup> The syndrome parallels gonorrheal infection so closely that suspicion of the gonococcus is difficult to dispel.

Urethritis has been reported in all cases of this disease. The anterior and posterior urethra are involved, often with cystitis. It resembles the usual gonorrheal infection. For this reason it is difficult to recognize it apart from gonorrhea unless smears have been repeatedly negative and the course of the disease has been followed until its later stages.

Conjunctivitis is a constant finding. It is acute in onset, purulent in character, usually with bilateral involvement. A tendency to spontaneous recovery without corneal ulceration is the rule. Keratitis and iritis have not been uncommon complications. The ocular symptoms ultimately subside, with full restoration of vision.

In the case reported a crop of small vesicles developed chiefly in the central area of the cornea five days after the onset of the conjunctivitis. These broke down shortly, to form discrete superficial ulcers which showed no tendency to coalesce or penetrate and healed without residual opacification within the ensuing three weeks. Photophobia was intense during this period. The iritis followed the keratitis after an interval of five days. It was of the

acute plastic variety and accompanied by hyphema at its onset. The involvement of the left eye was similar but milder in degree.

Chronic arthritis is ordinarily the severest complaint. More than one joint is usually involved and most frequently those of the toes, ankle, wrist and knee. The arthritis persists the longest but generally clears up in from one to five months, leaving no permanent stiffness or ankylosis.<sup>3</sup>

Cutaneous lesions may be simple erythemas, urticarial or erythema nodosum-like eruptions, hemorrhagic and vesicular eruptions or hyperkeratotic lesions. To the dermatologist, its chief interest lies in the keratotic cutaneous lesions which have appeared in roughly 40 per cent of the cases reported. The cutaneous manifestations have been typical or similar to those seen in keratosis blenorrhagica. Hence this syndrome has also been termed "keratosis blenorrhagica without gonorrhea".<sup>4</sup>

Forty-six of the cases reported have occurred in young men. One case has recently been reported in a white woman. Only one death has been reported<sup>1</sup>, it was attributed to a myocardial infarct. The disease cannot be distinguished from a gonorrheal infection clinically. Bacteriologic studies are the only means of differentiation. Failure to respond to sulfadiazine and penicillin also sets this syndrome apart. The course of the disease is usually milder, and complete recovery is the rule. Recurrences have been reported as late as six years after the original onset. The cause of Reiter's disease is unknown. No remedy has been found to be of specific benefit.

### REPORT OF A CASE

*History*—A man, aged 29, noticed a urethral discharge, purulent in character, on June 28, 1944, ten days after exposure. There was no history of previous urethral discharge. Three days later he sought the attention of a general practitioner who, without

1 Lever, W. F., and Crawford, G. M. Keratosis Blenorrhagica Without Gonorrhea (Reiter's Disease?), Arch Dermat & Syph 49 389 (June) 1944. Complete bibliography.

2 Reiter, H. Ueber einer bisher unbekannte Spirochaeteninfektion (Spirochaetosis arthritica), Deutsche med Wchnschr 42 1529, 1916.

3 Comroe, B. I. Arthritis and Allied Conditions, ed 2, Philadelphia, Lea & Febiger, 1941.

4 Buschke, A. Ueber die sog "Gonorrhoeischen Hyperkeratosen" ohne Gonorrhoe, Klin Wchnschr 7 1133, 1928.

taking a smear, prescribed eight (0.5 Gm) tablets of sulfathiazole daily and a medication to be used for urethral irrigation.

Some diminution in the quantity of discharge ensued during the next two weeks, at which time he was instructed to change to four (0.5 Gm) sulfadiazine tablets daily. During the next six days the urethral discharge subsided considerably, but on July 21, 1944 both eyes became congested. On the next day there was a profuse purulent discharge present in both eyes.

On July 23, 1944, the patient first came under our observation because of the intensity of the conjunctivitis. Examination disclosed intense congestion of the palpebral and bulbar conjunctiva of each eye associated with a purulent secretion. Mild edema of both upper lids was present. The patient complained of marked photophobia.

A short time after irrigation the conjunctival sac refilled with pus. Slit lamp study revealed no evidence of involvement of the cornea or iris.

*Laboratory Examination*—A smear was taken and sent directly to the laboratory, gonococcal conjunctivitis having been suspected because of the clinical appearance and the history of recent urethritis.

The laboratory gave the following report. The conjunctival smears were negative for intracellular or extracellular gram-negative cocci. In the urethral smears (three consecutive days) no intracellular gram-negative diplococci were found. The urethral culture, the blood culture, the culture of the cutaneous lesions and the culture of the synovial fluid of the right knee were negative for the gonococcus. The serologic reactions to the Kahn test were negative. The blood count (three days after admission) was: erythrocytes 4,790,000, hemoglobin 16.8 Gm, white blood cells 10,700, neutrophils 81, lymphocytes 13, monocytes 4, eosinophils 1 and basophils 1.

*Treatment and Course*—In spite of the laboratory report, again because of the history and clinical resemblance to blenorragic conjunctivitis, the patient was hospitalized and placed on the following medication: penicillin 20,000 units intramuscularly statim, to be repeated each four hours, conjunctival irrigations with boric acid solution every two hours. Twenty-four hours later, there being no improvement, ocular irrigations were ordered hourly, and 10 Gm of sulfadiazine orally were administered in divided doses. Since no improvement was noted the sulfadiazine and penicillin were discontinued after a total of 170,000 units had been administered. Nine days later another course of 100,000 units was administered within twenty-four hours, without benefit.

Three days after admission to the hospital the interphalangeal joints of the second and third toes became swollen and painful. During the next four days the right heel, third and fourth toes of the left foot, left wrist and right knee progressively were involved.

The conjunctival discharge and edema of the lids subsided slowly but steadily after admission to the hospital, but in no manner was the response similar to that usually seen when penicillin or sulfadiazine is used. Coincident with the onset of the arthritis a cluster of superficial vesicles was observed in the central area of each cornea. At this time the conjunctival congestion was still intense though the discharge had become scanty.

From July 26 to July 30, the patient's temperature ranged from 99 to 102 F. From July 31 to August 7, the temperature ranged from 98.6 in the morning to 102 in the evening. Thereafter the patient remained afebrile. Examination in this interval revealed a normal prostate.

On the tenth day of hospitalization, a marked ciliary flush developed in the right eye. Numerous corneal precipitates and a plastic exudate in the pupillary area overlying the anterior lens capsule appeared shortly thereafter.

On the thirteenth day in the hospital cutaneous lesions began to appear. These were hemorrhagic vesicular lesions, the size of a pea, two occurred on the lateral aspect of the left ankle, two on the dorsum of the right ankle, one on the left buttock and one on the right lumbar region. The lesions were rapidly transformed into keratotic elevations which lasted for four weeks, peeling off like crusts and leaving pale scars.

By the fifteenth day of hospitalization the iritis of the right eye had become steadily more severe and a mild iritis had developed in the left eye. Thereafter, a continuous gradual improvement of the keratitis and iritis ensued with complete subsidence of all ocular conditions on Sept. 3, 1944. Therapy consisted only of hot compresses and instillations of atropine.

Approximately two months after hospitalization all symptoms had disappeared.

#### SUMMARY

A case of Reiter's disease is presented chiefly because of the severity of the ocular complications. The ophthalmologist should be aware of this syndrome, which resembles a gonorrheal infection closely but is not due to the gonococcus. While therapy is nonspecific, the ultimate prognosis for the eyes is good.



# LOCAL TOXIC EFFECT OF DETERGENTS ON OCULAR STRUCTURES.

IRVING H. LEOPOLD, M.D., D.Sc.

PHILADELPHIA

In recent years attention has been directed to the value of detergents in ophthalmology. Although they are being used as germicides and cleansing agents,<sup>1</sup> most of the ophthalmologic consideration has been devoted to their penetrant action, i.e., to their ability to aid in increasing the penetration of therapeutically active substances through the cornea. O'Brien and Swan<sup>2</sup> demonstrated that the intraocular penetration of carbaminoylcholine chloride could be enhanced by the use of 0.1 per cent zephiran chloride, 1 per cent saponin, 0.1 per cent Duponol PC or 0.1 per cent Aerosol OT. Other investigators followed this lead and showed that the intraocular penetration of other locally applied drugs could be increased by the use of detergents. Bellows and Gutmann<sup>3</sup> demonstrated the increased penetration of sulfonamide compounds when such detergents as Aerosol OS, Aerosol OT, Tergitols 4, 7 and 08, Ocenol KD (oleyl alcohol), sodium lauryl sulfate and zephiran chloride were used. Leopold and Scheie<sup>4</sup> studied the increased penetration of sulfathiazole from liquid and ointment vehicles using 0.1 per cent Duponol ME dry, and Leopold and Steele<sup>5</sup> observed the increased penetration of other sulfonamide drugs, using 0.1 per cent Duponol ME dry in eyes with normal, inflamed and abraded corneas. Boyd<sup>6</sup> established the increased penetration of physostigmine with the employment of zephiran in the vehicle.

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1. Smith, C. S. Some Recent Advances in Ophthalmology, *J. Missouri M. A.* **36**:72, 1939.

2. O'Brien, C. S., and Swan, K. C. Carbaminoylcholine Chloride in the Treatment of Glaucoma Simplex, *Arch. Ophth.* **27**:253 (Feb.) 1942.

3. Bellows, J. G., and Gutmann, M. Application of Wetting Agents in Ophthalmology, *Arch. Ophth.* **30**:352 (Sept.) 1943.

4. Leopold, I. H., and Scheie, H. G. Studies with Microcrystalline Sulfathiazole, *Arch. Ophth.* **29**:811 (May) 1943.

5. Leopold, I. H., and Steele, W. H. Unpublished observations.

6. Boyd, J. L. Quantitative Comparison of Methods of Administering Physostigmine, *Arch. Ophth.* **30**:521 (Oct.) 1943.

It would seem advisable to consider the incorporation of these detergents in various ophthalmic preparations in an effort to increase the intraocular penetration of many locally applied therapeutic agents. However, before any medicinal agent can be recommended for local ocular use, its toxic properties must be determined. Maier<sup>7</sup> found little or no reaction from the daily application of zephiran chloride in concentrations of 1:4,000 to 1:2,500. He did notice defensive movements of the animal immediately after instillation. However, Maier washed out the zephiran with saline solution one minute after application. Swan<sup>8</sup> called attention to the local toxic effect of detergents, with particular reference to zephiran. He showed that minute concentrations of zephiran chloride as small as 0.025 per cent, resulted in a violent reaction in the rabbit eye when injected into the anterior chamber. Even more important was the development of conjunctival edema and desquamation when a single drop of a solution containing 0.1 per cent zephiran chloride was applied to the human cul-de-sac. After such a dose he also noted minute punctate gray areas, which tended to coalesce and form a gray haze in the corneal epithelium. Repeated instillations of zephiran chloride in a concentration as low as 0.03 per cent produced similar conjunctival and corneal changes. All changes, however, were reparable when application of the drug was stopped. Swan<sup>8</sup> also noted that the damage which followed local application of undiluted Aerosol OT was entirely superficial.

It has been shown that the bactericidal activity of standard antiseptics, such as chloramine-T, chlorazodin, merthiolate, and potassium permanganate, was enhanced when combined with wetting agents.<sup>9</sup>

Kintz<sup>10</sup> reported better results with sulfonamide compounds plus a detergent than with

7. Maier, E. Preservation of Biological Fluids, *J. Bact.* **38**:33, 1939.

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(Footnotes continued on next page)

sulfonamide solution alone against infected wounds of the soft tissues of the face Robson and Scott<sup>11</sup> demonstrated that a solution of sodium sulfacetamide or of sodium sulfadiazine plus 0.1 per cent Duponol ME dry was more effective in clearing standard experimental infections of the cornea due to the streptococcus than either sulfonamide preparation without the detergent

The local instillation of many drugs, such as the sulfonamide compounds, must be made several times each day for maximum effect In many instances the eyes requiring therapy will be abraded or have infected ulcerations Before recommending the incorporation of detergents in solution of a sulfonamide compound, it is necessary to determine the tolerance of eyes with corneal abrasions as well as of eyes with intact corneas, for the various detergents That is the purpose of the present studies

EXPERIMENTAL STUDY

METHODS AND MATERIAL

*Normal Rabbit Eyes*—The detergents which were studies are listed in table 1 Each agent was studied in concentrations of 0.1, 0.25, 0.5, 1 and 100 per cent Zephiran chloride was studied in 0.03 per cent concentration, as well as in the other concentrations Isotonic solution of sodium chloride was used as the diluent The  $p_H$  of the resultant solutions, as measured by a

TABLE 1—Synthetic Detergents Investigated \*

Aerosol OT	Dioctyl ester of sodium sulfosuccinate	American Cyanamid and Chemical Corporation
Aerosol OS	Isopropyl naphthalene sodium sulfonate	American Cyanamid and Chemical Corporation
Tergitols 4 and 7	Higher secondary alcohol sulfate	Carbide and Carbon Chemical Corporation
Tergitol 08	Synthetic primary alcohol sulfate	Carbide and Carbon Chemical Corporation
Zephiran	High molecular alkyl, dimethyl and benzyl ammonium chlorides	Alba Pharmaceutical Co., Inc
Duponol ME dry	Higher aliphatic alcohol sulfates derived from technical lauryl alcohol and contains a minimum of electrolytes	E I du Pont de Nemours & Co., Inc

\* All the data in this table except those for Duponol, are derived from Bellows and Gutmann<sup>3</sup>  
All the detergents except zephiran are anionic zephiran being cationic

glass electrode, ranged from 6 to 7.5 The  $p_H$  of the aerosols varied from 6 to 7 The Tergitol, Duponol and zephiran preparations had a  $p_H$  of about 7 Normal rabbit eyes were used in the first group of tolerance

10 Kintz, F P Traumatic Wounds of the Soft Tissues of the Face with a Preliminary Report on a New Azochloramid Solution and a New Sulfonamide Solution, Mil Surgeon 89 61, 1941

11 Robson, J M, and Scott, A A B Experimental Streptococcal Lesions of the Rabbit's Eye and Their Treatment, Brit J Exper Path 25 81, 1944

experiments All eyes were examined with the aid of a corneal biomicroscope The following methods of application were employed (1) single instillation of 2 drops of each concentration, (2) repeated instillation four times daily of each concentration except the undiluted strength

*Tolerance of Eyes with Abraded Corneas*—Mechanical denudations 6 mm in diameter were produced in the corneas of rabbit eyes by means of a trephine and plunger

TABLE 2—Influence of Detergents on Regeneration of Corneal Epithelium

Concentration of Detergent Used	Number of Eyes Whose Corneal Epithelium Had Regenerated on Designated Days							
	2	3	4	5	6	7	8	9
Tergitol 4, 0.5%			1			5	2	
Control		5	3					
Tergitol 4, 0.1%			2	1	2	1		
Control		3	2	1				
Tergitol 7, 0.5%			2	1	1	2		
Control		2	4					
Tergitol 7, 0.1%			3	3				
Control		5	3					
Tergitol 08, 0.5%			4		2			
Control		4	2					
Tergitol 08, 0.1%			4	1	1			
Control		3	2	1				
Zephiran chloride 0.1%				2	2	2		
Control		3	3					
Zephiran chloride, 0.03%			2	3	1			
Control		5	1	0				
Duponol ME dry, 0.5%			4	2	1	4		
Control		4	1	1				
Duponol ME dry, 0.1%			4	1	1			
Control		5	1	0				
Aerosol OS, 0.5%				1		1	4	
Control	1	3	2					
Aerosol OS 0.1%			2	1	3			
Control		5	3					
Aerosol OT 0.5%						2	2	2
Control	2	4		2	2			
Aerosol OT, 0.1%			2	2	2			
Control	1	2	5					

so arranged as to cut a constant depth The epithelium was removed from the cut area by means of a swab dipped in collodion Fluorescein was used as a guide to the depth and extent of staining This method has been previously described<sup>12</sup> Denudations were produced in this manner in both eyes of 84 chinchilla rabbits, weighing from 2 to 3 Kg All of the detergents listed in table 1 were used The concentrations used were 0.1 and 0.5 per cent of each of the following substances Duponol ME dry, Aerosol OS and OT and Tergitols 4, 7 and 08 Zephiran chloride was used in concentrations of 0.1 and 0.3 per cent Each solution to be tested was applied to the right eyes of 6 rabbits The left eyes of the 6 rabbits received isotonic solution of sodium chloride and acted as controls Instillations were made four times each twenty-four hours, at 9, 12, 3 and 6 o'clock Each instillation consisted of 4 drops Each eye was examined and stained with fluorescein daily The results are listed in table 2 Instillations were made for three days

RESULTS

*Normal Eyes*—Single instillations of all detergents except zephiran chloride in concentra-

12 Leopold, I H, and Steele, W H Influence of Locally Applied Sulfonamides and Their Vehicles on Corneal Epithelial Regeneration, Arch Ophth, to be published



tions of 0.1 per cent failed to produce any signs of corneal involvement or conjunctival injection in the normal eyes. All agents produced marked blepharospasm in this concentration. In 0.1 per cent concentration zephiran chloride produced conjunctival hyperemia, edema, loosening of the conjunctival epithelium and minute areas of corneal staining. These changes disappeared entirely within twenty-four hours.

Single instillations of 0.25 per cent concentrations of all the detergents tried except zephiran chloride failed to produce any corneal changes but did create slight conjunctival hyperemia. The changes noted with zephiran chloride in 0.25 per cent concentration were similar to those with 0.1 per cent concentration and also disappeared within twenty-four hours. Single instillations of 0.5 per cent concentrations of all the detergents produced all the conjunctival changes noted with 0.1 per cent zephiran chloride. These disappeared in twenty-four hours. Of these substances, Tergitol 08 produced the least changes. Only zephiran produced corneal alterations. The 1 per cent concentrations of all the detergents except Tergitol 08 produced blepharospasm, conjunctival hyperemia, edema, loosening of conjunctival epithelium, superficial corneal haziness and areas of corneal staining. All these changes disappeared within twenty-four hours after single applications. Tergitol 08 produced less pronounced conjunctival changes than the others and no corneal changes.

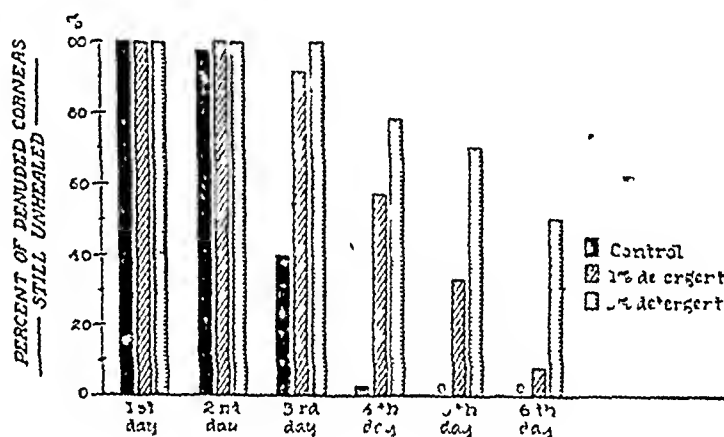
Single applications of the undiluted Tergitols 4, 7 and 08, of the powder of Duponol ME dry and Aerosol OS and of the solid aerosol OT produced marked conjunctival injection, edema, considerable sloughing of the conjunctival epithelium and staining of one third of the cornea within the first few minutes. Superficial punctate areas and corneal haziness occurred in all eyes. These changes had disappeared from the majority of the eyes so treated by the end of one week. A few eyes showed a slight corneal haze, although there was no corneal staining at the end of two weeks. Although some eyes recovered more rapidly than others, one agent when used in this concentration did not produce consistently less damage than the others. At no time did biomicroscopic examination reveal any pathologic change in the iris, the lens or the anterior chamber.

Repeated applications four times daily of 0.1 and 0.25 per cent concentrations of Duponol, Aerosol OS and Aerosol OT and Tergitols 4, 7 and 08 created only mild conjunctival injection. However, after each instillation considerable blepharospasm occurred, which persisted for ap-

proximately four minutes. These conjunctival changes disappeared entirely within twenty-four hours after the instillations were discontinued.

Repeated use of 0.5 per cent concentrations of Duponol ME dry, Aerosol OT, Aerosol OS and Tergitols 4 and 7 produced pronounced conjunctival edema, sloughing of epithelium and hyperemia. A mucoid discharge also developed. Corneal staining and superficial haziness occurred. All eyes cleared within forty-eight hours after the therapy was stopped. Tergitol 08 did not produce these changes in this concentration after five days of such therapy. With all the other detergents these changes developed after twenty-four hours.

Repeated use of a 1 per cent concentration of each agent produced the same changes. These were more severe and did not fully disappear in all eyes until seventy-two hours had elapsed after cessation of therapy. Tergitol 08 produced the corneal changes in this concentration only after seven days of such treatment.



Influence of detergents on regeneration of the corneal epithelium

The following detergents were used in the study in both 0.5 and 0.1 per cent concentration: Tergitols 4, 7 and 08, aerosols OS and OT, and Duponol ME dry. Zephiran chloride was used in 0.1 per cent concentration only.

There were 84 control eyes, 36 eyes were treated with the 0.5 per cent concentration and 42 eyes with the 0.1 per cent concentration.

**Abraded Eyes**—Table 2 and the graph present the results of experiments on epithelial regeneration. It is evident from the data that all these agents retard regeneration of corneal epithelium when 0.5 per cent concentrations are used four times a day. The 0.1 per cent concentrations also retard regeneration of corneal epithelium, but not to such a degree as the 0.5 per cent preparations. Zephiran chloride retards regeneration of corneal epithelium slightly in concentrations as low as 0.03 per cent. In many of the abraded eyes receiving a 0.5 per cent concentration of the detergent four times a day, vascularization and edema of the cornea occurred.

A few became infected in spite of the bactericidal potentialities of the detergents. Scarring occurred in a few of the detergent-treated eyes but not in any of the control eyes.

#### COMMENT

It is evident that the detergents are capable of inflicting damage to normal rabbit eyes. Concentrations which are damaging vary with the detergent and with the frequency of application. The damage, as pointed out by Swan,<sup>8</sup> is entirely superficial even when an undiluted preparation of the detergent is used. The structures involved are the conjunctiva and the cornea. Conjunctival edema, mucoid discharge, sloughing of cells and injection are characteristic. Punctate haziness, and later general haziness and staining, of the cornea are found. These changes are similar to those described by Swan.<sup>8</sup> The tissue alterations noted in the normal rabbit eye are usually capable of recovering without permanent damage after contact with the detergent is ended. No change characteristic of an individual detergent was noted. All the detergents tested produced the same type of ocular damage.

All detergents used retarded regeneration of corneal epithelium. This retardation was marked when a solution containing 0.5 per cent of the detergent was used. The 0.1 per cent concentration of each detergent still retarded epithelial regeneration although much less so than the higher concentration.

Various suggestions have been made to account for the cytotoxic effects of detergents.

Loeb,<sup>13</sup> in 1913, found that surface-active agents, among them bile salts and higher fatty acids, when applied to unfertilized eggs of the sea urchin, induced cleavage and development, whereas higher concentrations caused cytolysis. Mirsky<sup>14</sup> and Anson<sup>15</sup> suggested that the protein molecules of the cells may be disrupted by the pull of the detergents and thus denatured. Kuhn and Beilig<sup>16</sup> suggested that the germicidal concentrations of some detergents correspond rather closely with the concentration necessary to bring about denaturation of proteins. Baker, Harrison and Miller<sup>17</sup> showed that there is a

fairly good correlation between the bactericidal action and the inhibition of bacterial metabolism. They were also able to demonstrate<sup>18</sup> that lecithin and cephalin could prevent this inhibition.

These studies do not contraindicate the use of detergents, they simply call attention to the toxic property of these compounds. These data would argue against universal incorporation of these agents in ophthalmic preparations. From these observations on their influence on rabbit eyes, one can say that detergents should not be recommended for repeated use in eyes with corneal abrasions. If they are used, the concentration should not be above 0.1 per cent for Duponol ME dry, Tergitol 08, Tergitol 4, Tergitol 7, Aerosol OS and Aerosol OT. Zephiran chloride could not be used in concentrations over 0.03 per cent. If detergents are used in eyes with an intact cornea, or wherever they are used, the patient should be warned to expect irritation and blepharospasm. All patients using local detergents in the eye, or ophthalmic preparations for local use containing detergents, should be examined at routine intervals to determine whether any local toxic effects of the detergent are appearing. Cessation of the use of the detergent will probably be followed by clearing of the superficial damage inflicted.

#### SUMMARY AND CONCLUSIONS

Repeated application of detergent solutions produced conjunctival damage in concentrations as low as 0.1 per cent. Zephiran chloride in this concentration produced corneal damage.

Repeated applications of higher concentrations of all the detergents tested produced superficial corneal changes in normal rabbit eyes.

Repeated applications of solutions containing 0.5 per cent of each detergent definitely retarded regeneration of corneal epithelium. The 0.1 per cent concentration slightly retarded the regeneration.

The changes produced in the conjunctiva and cornea by one application of undiluted preparations of several of the detergents are reparable.

The tissues subject to damage by the detergents are the conjunctiva and cornea. No evidence of involvement of deeper tissues of the cornea, the iris, the lens or the anterior chamber could be noted.

Local ophthalmic use of the detergents should be considered and recommended only with knowledge of their possible toxic properties.

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13 Loeb, J. *Artificial Parthenogenesis and Fertilization*, Chicago, University of Chicago Press, 1913.

14 Mirsky, A. E., in *Cold Spring Harbor Symposia on Quantitative Biology*, Cold Spring Harbor, L. I., The Biological Laboratory, 1938, vol. 6, p. 150.

15 Anson, M. L. *The Denaturation of Proteins by Synthetic Detergents and Bile Salts*, *J. Gen. Physiol.* 23: 239, 1939.

16 Kuhn, R., and Beilig, H. J. *Ber. d. deutsch. chem. Gesellsch.* 73: 1080, 1940.

17 Baker, Z., Harrison, R. W., and Miller, B. F. *The Bactericidal Action of Synthetic Detergents*, *J. Exper. Med.* 74: 611, 1941.

18 Baker, Z., Harrison, W., and Miller, B. F. *Inhibition by Phospholipids of the Action of Synthetic Detergents on Bacteria*, *J. Exper. Med.* 74: 621, 1941.

# PLASTIC SURGICAL REPAIR ABOUT THE EYE WITH FREE GRAFTS

MAJOR ABRAHAM SCHULTZ AND LIEUTENANT CHARLES  
MEDICAL CORPS, ARMY OF THE UNITED STATES

The surgical correction of scarred deformities about the eyes as the result of previous injuries assumes increasing importance to the military ophthalmologist as the war progresses. In their repair, special attention must constantly be given to the functional result of the eye, as well as to its cosmetic appearance. Because of his special knowledge of the physiology and anatomy of the eye and its adnexa, plastic surgical procedures about the eye are preferably performed by the properly trained ophthalmic surgeon.

In many instances, free grafts of skin or mucosa are most effective in accomplishing the desired result. This report cites 3 cases to illustrate the cosmetic and functional improvement about the eyes that can be obtained with use of various types of free grafts. It also serves to review and emphasize the important basic principle of these procedures as advocated by Wheeler and Hughes in the application of this form of plastic surgery.

## FREE MUCOUS MEMBRANE GRAFTS

Severe symblepharon may produce deformity, loss of vision or mechanical irritation of the eye. Its basis is loss of substance and consequent defect in the conjunctiva, followed by adhesions of the raw surfaces. Prior to the use of free grafts, surgical measures for relief from symblepharon often consisted simply of division of the band, sometimes with the use of a form, with the hope that this would prevent the adhesion from reforming. This procedure was unsuccessful since it did not attack the cause of adhesions.

The correction of symblepharon in cases in which there is insufficient conjunctiva to permit mobilization and covering of all raw surfaces without obliterating any of the fornix depends on replacing the lost substances with a graft. In his book on "Reconstructive Surgery of the Eyelids," Hughes<sup>1</sup> reviews the types of tissue which have been employed to repair conjunctival defects. These include, in the order of their first use: skin, rabbit conjunctiva, mucous membrane

from the mouth, human conjunctiva, autogenous vaginal mucosa, rectal mucosa, homogenous vaginal mucosa and homogenous amnion. Mucosa from the mouth, first used by von Carion in 1873, is now favored by most ophthalmic surgeons to repair defects of conjunctiva when the globe is present.

Autogenous buccal or labial mucosa grafts to the lids and globe take readily. The donor tissue is readily available and conveniently obtained, and the donor site requires little postoperative attention. It may be left unsutured. These advantages are of particular significance in military surgery. Unlike skin, mucous membrane provides a smooth surface and glands. It does not desquamate and has no hairs, therefore it does not produce corneal abrasion.

The technic of removal of the mucosa graft consists in raising a thin layer with superficial injection of procaine and dissecting with cataract knife or scissors. Any submucosal fat present on the graft is trimmed with scissors. The graft is promptly applied to the area of defect and sutured in place with fine silk sutures on atraumatic needles. When the graft is applied to the globe, it is desirable to fix it in place with episcleral sutures. This fixation has been emphasized by Gifford<sup>2</sup> and Castroviejo.<sup>3</sup> It is especially important at the limbus. Failure to do this may result in the graft growing over the cornea when tissue has been shaved from that structure, as in cases of recurrent pterygium.

### CASE 1—Mucous membrane graft for symblepharon.

G. M., a private aged 21, a member of a hospital medical detachment, was first seen in the eye clinic of Lovell General Hospital Feb. 2, 1943. He complained that for several months his right eye had been red, irritable and sensitive to light. This symptom was so severe on waking that he was unable to open the eye for thirty minutes or so, and then he squinted the lids of this eye most of the day.

He stated that at 9 years of age the right eye was burned with wet lime. Prompt treatment at an ophthalmic hospital saved the eye, but adhesions developed between the lids and the globe. Operation was subse-

2 Gifford, S. R. Lectures on Ophthalmic Surgery, Postgraduate Course in Ophthalmology, Northwestern University, 1941.

3 Castroviejo, R. Superficial Keratectomy, demonstrated by movies before the Washington, D. C., Ophthalmological Society, March 1944.

From the Eye Section, Lovell General Hospital, Fort Devens, Mass.

1 Hughes, W. L. Reconstructive Surgery of the Eyelids, St. Louis, C. V. Mosby Company, 1943.

quently performed for this defect, but no permanent improvement was obtained. After the accident, the injured eye became "practically blind," and the upper lid drooped. This condition had persisted unchanged.

Examination revealed that vision in the right eye was limited to perception of hand movements, visual acuity in the left eye was 20/20. The right upper lid drooped notably, and its movement was partially limited. The normal fold in the skin of the upper lid was absent. The bulbar conjunctiva was moderately injected. The upper fornix was largely obliterated by three adhesions between the lid and the globe (fig 1A). The largest of these extended from the midtarsal region down over the cornea to about 1 mm below its vertex, involving about 20 per cent of the corneal surface. The cornea presented an annular limbal opacity and numerous vascularized scars, of varying density, involving the anterior stroma and Bowman's membrane. The fundus was not visible. The results of examination of this eye were otherwise without significance. The left eye was normal.

Despite conservative medical treatment, the symptoms did not improve significantly during the ensuing year. It was thought that the symptoms were largely attributable to traction on the globe during movement.



Fig 1 (case 1)—Appearance of the lids (A) before and (B) after plastic repair.

To free the globe from the lid and to correct the disfigurement, surgical intervention was considered indicated.

On Jan 20, 1944, with local anesthesia, the scar was dissected from the cornea and sclera in one piece, without excising it. The bulbar conjunctiva on either side was incised a few millimeters from the limbus and dissection carried upward to form a fornix. All of this tissue was used to line the upper lid and to reconstruct the fornix. The large defect in the bulbar conjunctiva which resulted was repaired with a mucous membrane graft, 28 by 15 mm, obtained from the lower lip. This was held in place with episcleral, 000000 surgical silk placed around all its edges and with one suture in the center of the graft. A pressure dressing was applied, and both eyes were bandaged.

The eye operated on was first dressed four days later, and the fellow eye was thereafter left open. The sutures were removed over the period of from the sixth to the twelfth postoperative day, two or three sutures in the fornix being inaccessible before the twelfth day. The soldier returned to full duty on February 1. Since then there have been no symptoms. The conjunctival injection has cleared considerably. The ptosis is appreciably reduced and the normal fold has appeared in the skin of the lid. The upper

fornix is normal in depth (fig 1B). The globe and the lid move freely. The upper portion of the cornea, from which the adhesion was dissected, is now clearer than most of the rest of the cornea. The visual acuity is 20/300.

The relief of symptoms, the improvement of vision and the improvement of his appearance have had a salutary effect on this soldier's morale and have permitted him to perform his duties without the interruptions previously necessitated by visits to the clinic. As was pointed out by Spaeth,<sup>4</sup> mucous membrane grafts in the repair of such conditions may preserve "the possibility of future improvement in vision by keratoplasty."

#### FREE EPITHELIAL GRAFTS

This type of graft was first reported by Ollier in 1872 and modified by Thiersch in 1874 so that it is now generally known as the Ollier-Thiersch graft. It includes the epidermis and tops of the papillae of the corium and averages 0.01 inch (2.5 mm) in thickness. It is preferably taken from the hairless surfaces of the inner thigh or arm with a large razor or with the Padgett dermatome. Because of its great availability and high probability of take, it may be used in repair of large traumatic defects or extensive granulation surfaces of the lids. Because of its thinness, however, the epithelial graft appears blanched and offers less protection than a full thickness graft.

One of the chief uses of the Ollier-Thiersch graft today is in epithelization of the eye socket. The procedure was first reported by Esser<sup>5</sup> in 1917. It was then further modified until it was perfected by Wheeler<sup>6</sup>. He stressed the following points to be observed in relining the orbit:

- 1 Wide excision of the scar tissue causing contraction of the eye socket.

- 2 Careful dissection of the scar tissue from the under surface of the lids, with especial care to avoid injury to the levator palpebrae muscle.

- 3 Reconstruction of fornices with the incision extended to the lower orbital rim.

- 4 Use of a mold, carefully shaped to fit the orbit, about which the graft is wrapped with the raw surface outward.

- 5 Complete immobilization of the graft by application of a pressure bandage.

In taking the graft, the skin should be kept on the stretch and flat. The donor site is dressed with petrolatum gauze, and the first redressing is done on the fourth postoperative day. The

4 Spaeth, E. B. The Use of Mucous Membrane Grafts in Ophthalmic Plastic Surgery, *Am J Ophth* 20: 897-907, 1937.

5 Esser, J. F. S. Studies in Plastic Surgery of the Face, *Ann Surg* 65: 297-315, 1917.

6 Wheeler, J. M. Restoration of the Obliterated Eye Socket, *Am J Ophth* 4: 481-488, 1921.

newly formed skin may be retaken after three to four weeks, if necessary, if a Padgett dermatome is used

#### CASE 2—Thiersch graft of the orbit

W. E., a private aged 33, was admitted to Lovell General Hospital Feb 26, 1943 for plastic repair of the right orbit. Enucleation of the patient's right eye had been performed thirteen years previously, after a penetrating wound resulting from the accidental explosion of his rifle while hunting. An artificial eye, however, could never be retained in the socket because of secondary scar tissue.

On admission the socket of the right eye was shallow and conspicuously scarred. Thick adhesions extended from the fundus to the lower lid and partially obliterated the inferior cul-de-sac. This prevented proper retention of any prosthesis. The left eye was normal, and visual acuity was 20/40, correctible to 20/20.

On March 2, 1943 the scar tissue which was obliterating the eye socket was excised, with local anesthesia. The dissection was continued to the periosteum of the inferior orbital rim, thus freeing the lower fornix. The resulting raw surface was then made smooth in preparation for the skin graft, and all bleeding was controlled. A lateral canthotomy was done to facilitate the introduction and withdrawal of a mold of dental wax. This mold was carefully shaped to fit the socket, so that accurate contact between the opposing surfaces of the recipient area and the mold was made. A Thiersch graft, about 2 by 3 inches (5 by 7.5 cm) square, was cut from the inner surface of the right thigh with a Sheehan-Kilner knife. The epithelial graft was wrapped around the previously fashioned mold, with the raw surface outward, and inserted into the prepared bed of the socket, with the overlapping edges meeting at the palpebral fissure. The lids were then closed with three silk marginal mattress sutures. A pressure bandage was applied over the right orbit, and both eyes were kept covered eight days to insure complete immobilization of the graft. The lid sutures were removed on the tenth postoperative day, and the mold was removed. The epithelium was now adherent at all points of contact with the previous raw surface, and the lower fornix was well formed. All excess portions of the skin graft were trimmed and the desquamated material was removed from the socket daily by irrigation with a solution of boric acid. A temporary prosthesis was procured on the fifteenth postoperative day and was satisfactorily retained in the restored socket. The patient was then returned to duty. Subsequently, a larger, permanent prosthesis was obtained.

#### FREE FULL THICKNESS GRAFTS

The military surgeon will often be able to reduce the need for plastic procedures by proper technic in the initial repair of lacerations of the lids. This involves complete hemostasis, careful approximation of all wound lips and particular attention to the lid margin. The white line and the anterior and posterior borders of the lid margins should be precisely aligned and sutured. The tongue and groove technic of Hughes<sup>7</sup> with intermarginal sutures or adhesions, is recommended. If the laceration is small, the intra-

marginal suture of Minsky<sup>8</sup> may suffice and is perhaps particularly useful for the average military surgeon.

The repair of defects of the skin of the lid was first accomplished with sliding flaps and pedicle grafts. The use of structures of one lid for the repair of the opposing lid was first advocated and instituted by Grandenigo in 1870. The first successful use of free, full thickness skin for a defect of the skin of the lid was made by Le Fort in 1872 in a case of ectropion. At the same time, he employed the all-important principle of partial closure of the lids to prevent postoperative contraction.

Full thickness skin has been obtained from various parts of the body, including chiefly the arm, the leg and the back of the ear. Use of the skin of the upper lid was first emphasized by Dantelle and Taitois in 1918. This technic was perfected by Wheeler,<sup>9</sup> who stated that in the young adult a piece of skin 20 to 25 by 50 mm might be removed from the upper lid without danger of lagophthalmos. Skin from the lower lid should not be used because of the danger of producing ectropion.

Skin from the lid is superior to skin from any other source. In contrast to other skin, it gives a good, if not perfect, match in all respects—hair, color, texture, thickness and flexibility. There is little subcutaneous tissue. The graft does not tend to contract. The donor site is closed without difficulty with a subcuticular suture and heals without scar, deformity or loss of function. When a defect cannot be satisfactorily repaired with a free, full thickness graft, a sliding or pedicle flap may sometimes be utilized. Such grafts, however, which are taken from the brow or the cheek, have the disadvantages of greater thickness of the skin, increased scarring at the edge of the graft and new scars in the donor area.

The free, full thickness graft is outlined on the donor lid with a knife and dissected with cataract knife or scissors, taking care not to include any deep tissue. It is important to avoid handling the tissue, especially with forceps. A few sutures, preferably one in each end, may be placed for traction. These same sutures are used to fix the graft in its new site. There it is placed in a bed which has been carefully prepared, all scar tissue having been removed and all bleeding stopped. Fine sutures are placed close to the edge. Intermarginal adhesions are employed to

<sup>8</sup> Minsky, H. Surgical Repair of Recent Lid Lacerations. Intramarginal Splinting Suture, Surg. Gynec. & Obst. **75**:449-456, 1942.

<sup>9</sup> Wheeler, J. M. Correction of Cicatricial Ectropion by the Use of True Skin of Upper Lid, J. A. M. A. **77**:1628-1630 (Nov. 19) 1921.



splint the repaired lid and to keep it on the stretch after operation

In the hands of some operators, free, full thickness grafts have not been highly successful Padgett<sup>10</sup> referred repeatedly to failure of take of full thickness grafts, but he also mentioned the suitability of full thickness skin from the lid for repair of defects of the lid. The problem in the case of repair of the lids differs from that in general plastic procedures, in that full thickness skin from the lid is thin, the area to be grafted

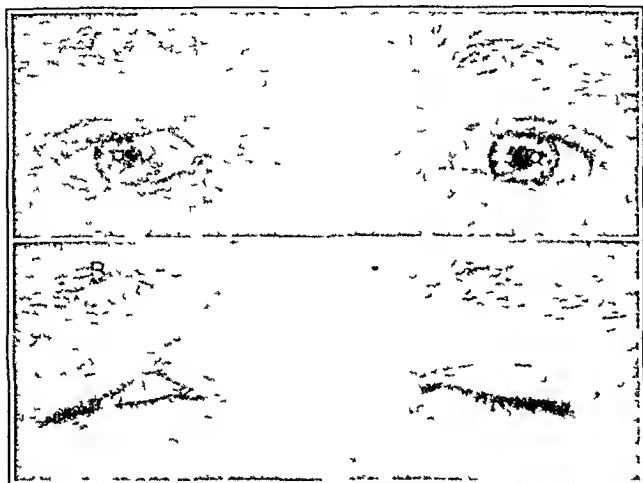


Fig 2 (case 3) —Appearance of the lids before plastic repair, with the eyes (A) open and (B) closed

is relatively small and the base is less often a granulating surface, which is a less favorable base for full thickness grafts. Furthermore, the ophthalmologist, in his grafting, probably less often deals with patients suffering from dehydration, hypoproteinemia and avitaminosis.

In the case of skin from the lid, free, full thickness grafts usually take when utilized by operators who have followed the principles set down by Wheeler. He emphasized the importance of pressure dressing, providing close application and immobilization and preventing edema and exudate. A stent may be desirable. Sea sponge, if available, is useful in obtaining pressure but is not necessary. Wheeler did not change the first dressing for five to seven days. Subsequent dressings are made at intervals of two to five days. A rise in temperature, pain, odor and discharge at the edge of the dressing will permit the diagnosis of infection if it is present. The graft need not be disturbed by early and frequent dressings.

#### CASE 3—Repair of defect of skin of lid

A V, private first class, was admitted to Lovell General Hospital March 15, 1944, complaining of inability to close his right eye completely, associated with redness and discharge in that eye.

<sup>10</sup> Padgett, E C. *Skin Grafting*, Springfield, Ill., Charles C Thomas, Publisher, 1942, pp 20, 25 and 85.

He stated that on Jan 23, 1944 he sustained multiple lacerations about the face, when he was thrown through the windshield of an automobile involved in a collision. He had received prompt treatment at another hospital, including cutaneous sutures for lacerations of the right upper eyelid, the right eyebrow, the right cheek and the scalp.

On examination, the right upper lid was seen to be pulled up and away from the globe by a scar running from the junction of the medial one quarter and the lateral three quarters of the border of the lid to a point about 8 mm above the eyebrow (fig 2A). The lid did not follow the eye on downward gaze. The borders of the upper and lower lids of the right eye did not meet from the middle of the lids to the medial canthus, when the eyes were closed (fig 2B). The exposed conjunctiva of the globe in this region was injected. The medial quarter of the border of the upper lid was slightly everted. An attempt to evert the upper lid showed that the medial end of the tarsus was fixed by the scar below the eyebrow. There was no limitation of motion of either eye.

On March 20, 1944 the scar tissue of the right upper lid was completely excised. To form adhesions to the lid, the lid margins at this site were denuded in two pairs of opposing areas and brought together by means of mattress sutures tied over rubber bolsters. The defect in the skin in the right upper lid was repaired with a free, full thickness graft, elliptic in shape and measuring 25 by 9 mm, taken from the left upper lid. The graft was sutured in place with closely spaced, fine, interrupted silk sutures on atraumatic needles. The surgical wound of the donor lid was closed with a subcuticular, running silk suture. Both eyes were dressed, and a pressure bandage was applied to the right eye.

The first dressing was done on the fifth day. The subcuticular suture was then removed from the left



Fig 3 (case 3) —Appearance of the lids after plastic repair, with the eyes (A) open and (B) closed

lid and the right eye only dressed. All sutures were removed from the right lid on the seventh day. A pressure dressing on the right eye was continued for eleven days. All dressings were discontinued on the sixteenth day. The intermarginal adhesions were left in place for two months and then severed.

At the time of this report, three months after operation, the lid is in good position, and the coloboma is absent (fig 3A), the lid follows the eye on downward gaze and meets well on closure (fig 3B).

# POSTERIOR PRINCIPAL PLANE OF THE OPTICAL SYSTEM OF THE EYE AND SIGNIFICANCE FOR REFRACTION

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Refraction in the eye is determined by the position of the posterior focus of the eye in relation to the retina, which, in turn, depends on the length of axis and on the value of separate elements in the refractive apparatus of the eye, namely, radiuses of curvature of the cornea and of the surfaces of the lens, depth of the anterior chamber and thickness of the lens. The results of my investigations, described in a number of papers,<sup>1</sup> have shown that the length of the axis, as well as the elements of the refractive apparatus, vary considerably and that this variability has a great, and sometimes decisive, significance for refraction, permitting one to evaluate properly a number of peculiarities associated with the anomalies of refraction. However, the length of axis and its significance for refraction are not the only factors determining refraction in the eye. The position of the principal plane of the optical system is also of great importance. Each optical system possesses a definite refractive power. But if one takes into consideration that the distance of the posterior focus of the eye is measured from the principal planes of the optical system, it is clear that the position of the posterior focus must depend not only on the refractive power of the system but on the position of the principal planes. For this reason, the position of the posterior focus in two optical systems possessing the same refractive power may be different, depending on the position of the principal planes. When applied to the optical system of the eye, this means that the position of the posterior focus depends both on the refractive power of the eye and on the position of the posterior principal plane of the visual optical system. The greater the distance between the cornea and the posterior principal plane of the eye, the more the posterior focus will be displaced backward, the refractive power of the optical system remaining the same, on the other hand, the smaller the distance between the cornea and the

posterior principal plane, the more forward will be the posterior focus of the optical system. It follows that the position of the chief posterior focus in relation to the retina and consequently the refraction differ with the same length of axis and refractive power, depending on the position of the posterior principal plane of the optical system.

The aim of the present study was to determine whether or not the foregoing statements concerning the significance of the posterior principal plane of the eye in refraction are true. The verification was made with 275 eyes by measuring the refraction with the Tscherning ophthalmophakometer (refraction from +10 to -25 D). The radius of corneal curvature was measured with the Javal ophthalmometer. The radiuses of curvature of the surfaces of the lens, the depth of the anterior chamber and the thickness of the lens were measured with the Tscherning ophthalmophakometer. The position of the posterior focus and the length of axis were calculated on the basis of the data obtained from these determinations after refraction under atropine cycloplegia. Measurements of 130 eyes were taken by my associates and me, and values for 145 eyes were obtained from the works of Averbakh<sup>2</sup> and Zeeman<sup>3</sup>. I used the same material in a number of my earlier investigations.

The first problem to be investigated is the variability of the position of the posterior principal plane of the optical system. It is well known that Gullstrand calculated for his schematic eye a distance of 1602 mm between the principal posterior plane and the cornea. Our data are given in table 1.

As can be seen from this table, the position of the posterior principal plane in the optical system of the eye varies widely, within the limits of 106 and 251 mm. Its average distance from the cornea is 163 mm. Thus, our average value co-

1 Tron, E. Optical Bases of Ametropia, in Special Collection on Ophthalmology in Honor of Forty Years of Scientific Activity of M. I. Averbakh, Moscow, Gosudarstvennoe izdatelstvo biologicheskoy i meditsinskoy literature, 1935, Optic Foundations of Aniso- and Isometropia, *Sovet vestnik oftal* 6 481-499, 1935.

2 Averbakh, M. I. Dioptrics of Eyes with Various Refraction, Inaug. Dissert., Moscow, 1900.

3 Zeeman, W. P. C. Ein Beitrag zur Frage der optischen Grundlagen der Aniso- und Isometropie, *Arch f Ophth* 133 211-230, 1935.



incides with the position of the posterior principal plane in Gullstrand's schematic eye. However, significant deviations from this average value in either direction have been recorded. Values of 1.40 to 1.90 mm have been frequently encountered, namely, in 232 eyes (84.5 per cent).

It is seen from the literature that investigations were carried out sixty-five years ago the results of which permitted the conclusion that the position of the posterior principal plane in the optical system of the eye is subject to considerable variations. After Helmholtz had suggested his oph-

TABLE 1—Position of Posterior Principal Plane in 275 Eyes with Refraction from +10.0 to -25.0 D

Position of Posterior Principal Plane, Mm	Number of Cases
1.00 to 1.09	1
1.10 to 1.19	1
1.20 to 1.29	6
1.30 to 1.39	17
1.40 to 1.49	48
1.50 to 1.59	52
1.60 to 1.69	62
1.70 to 1.79	38
1.80 to 1.89	32
1.90 to 1.99	9
2.00 to 2.09	5
2.10 to 2.19	2
2.20 to 2.29	
2.30 to 2.39	
2.40 to 2.49	1
2.50 to 2.59	1

thalmometer, a number of investigators were for many years engaged in measurements of elements of the visual apparatus of the eye. The difficulty of the method and the complexity and minuteness of the calculations restricted the number of examined eyes with various refractions to 56, among which 31 eyes had refractions from +5.5 to -13.0 D (measured by von Reuss<sup>4</sup>). The table shows that in 31 cases the position of the posterior principal plane of the optical system presented variations from 1.39 to 2.33 mm. However, von Reuss, citing these data, among other results of his measurements, did not emphasize the considerable variability in the position of the principal posterior plane as seen from these values and did not discuss the finding. The literature devoted to the investigation of the optical elements of the eye does not contain much on this subject, and the problem remains unsolved.

In order to determine factors influencing the position of the posterior principal plane in the

eye, we studied the correlation between this position and other elements of the optical visual apparatus. For this, we calculated the coefficient of correlation between the aforementioned elements. In estimating the data obtained, one must take into consideration variations of the coefficient of correlation from 0 to 1. A coefficient of correlation equal to 0 indicates that no quantitative interdependence exists between the two given values. A coefficient of correlation equal to 1 indicates a maximum possibility of interdependence between the two values. The correlation may be of two kinds: positive or negative. A positive correlation means a simultaneous increase of both values. A negative correlation means a converse process, that is, an increase of one value is accompanied with a decrease of the other. The error in the coefficient of correlation was also calculated in each individual case. This was done in order to establish the extent of accuracy of the coefficient. According to the rules of variation statistics, the coefficient of correlation is considered accurate only if the error is not more than one-third the value of the coefficient.

The coefficients of correlation obtained are given in table 2.

As may be seen in table 2, the coefficients of correlation show no interdependence between the posterior principal plane and the length of axis because there is only insignificant and inaccurate correlation between these two values (coefficient of correlation = 0.09, which is equal

TABLE 2—Correlation Between Posterior Principal Plane and Some Optical Elements of Visual Apparatus

Elements in Regard to Which the Coefficient of Correlation Was Calculated	Coefficient of Correlation
Length of axis	-0.09±0.08
Refractive power of eye	0.54±0.06
Refractive power of cornea	-0.002±0.08
Refractive power of lens	0.63±0.05

to the error ±0.08). This differs from the positive, and quite accurate, correlation between the position of the posterior principal plane and the refractive power of the eye (coefficient of correlation, 0.54 ± 0.06) and shows that the greater the refractive power of the eye, the farther the posterior principal plane is situated from the cornea. The refractive power of the eye is composed of two essential elements: the refractive power of the cornea and the refractive power of the lens. The refractive power of the cornea has no effect on the position of the posterior principal

<sup>4</sup> von Reuss, A. Untersuchungen über die optischen Constanten ametropischer Augen, Arch f Ophth 23 (pt 4) 183-268, 1877; Ophthalmometrische Mittheilungen 2. Messung eines atropinisirten hypermetropischen Auges, ibid 26 (pt 3) 7-11, 1880.

plane if the corresponding coefficient of correlation approaches 0 (0.02). It is quite different with the lens. A considerable, positive and quite accurate correlation (coefficient of correlation  $0.63 \pm 0.05$ ) between the position of the posterior principal plane and the refractive power of the lens indicates that the greater the refractive power of the lens the farther the posterior principal plane is situated from the cornea.

The foregoing data on factors determining various positions of the posterior principal plane in the optical visual system lead to the conclusion that changes in the position of the posterior principal plane in the eye are dependent on the value of the refractive power of the lens and that variations in this refractive power are most important.

TABLE 3—Position of Posterior Principal Plane in Eyes with Various Refractive Errors

Material	Number of Eyes	Extreme Variants, Mm	Average Value, Mm	Mean Square Deviation
All eyes	275	1.06 — 2.51	$1.63 \pm 0.01$	$\pm 0.20 \pm 0.01$
Emmetropia	60	1.30 — 2.51	$1.69 \pm 0.03$	$\pm 0.23 \pm 0.02$
Ametropia	215	1.06 — 2.18	$1.61 \pm 0.01$	$\pm 0.81 \pm 0.01$
Hypermetropia	95	1.07 — 2.06	$1.62 \pm 0.02$	$\pm 0.18 \pm 0.01$
Myopia	120	1.13 — 2.18	$1.60 \pm 0.02$	$\pm 0.18 \pm 0.01$

The position of the posterior principal plane of the optical visual system with various kinds of refractive anomalies is given in table 3.

As may be seen from table 3, the position of the posterior principal plane with various refractive conditions is the same. It is to be emphasized, however, that not only are the average values the same but the variability in the position of the posterior principal plane does not change if the mean square deviation is considered as the index of this variability.

Since the position of the posterior principal plane is subject to considerable changes, the question arises concerning the significance of this variability for ocular refraction. In the beginning of this paper, I suggested the hypothesis that, the length of axis and the refractive power of the eye being the same, the position of the posterior principal plane in relation to the retina, and consequently the refraction, should differ, depending on the position of the posterior principal plane. My associates and I carried out a detailed examination of 275 eyes, and in numbers of instances this hypothesis proved true. In the 4 cases in table 4 ametropia was produced by the position of the posterior principal plane.

In each of the 4 cases listed in table 4, two eyes are concerned: one emmetropic and the other

myopic. The refractive power and the length of axis are the same. The only difference is in the position of the posterior principal plane, the latter causing ametropia in these cases. Certain facts prove that this is really true. Namely, in each of these cases the posterior principal plane has displaced farther forward in the myopic eye than in the emmetropic one. This forward displacement of the posterior principal plane, the value for refractive power and the constant length of axis are the reasons that the principal focus is not situated on the retina but is in front of it, thus causing myopia. Consequently, the greater the difference in the position of the posterior principal plane, the greater the degree of myopia. Thus, myopia of 1.0 D (cases 1 and 2) corresponds to a difference in the position of the posterior principal plane of 0.39 and 0.36 mm, and myopia of 3.0 D (cases 3 and 4), to a difference of 0.88 and 0.92 mm respectively. It is to be noted, in addition, that difference in the position of the posterior principal plane corresponds to the degree of myopia. Forward dis-

TABLE 4—Ametropia Produced by Position of Posterior Principal Plane

Case Number	Change in Refraction, D	Length of Axis, Mm	Refractive Power of Eye, Mm	Principal Posterior Plane, Mm
1	— 1.0	23.42	62.20	1.59
	Emmetropia	23.49	62.10	1.98
2	— 1.0	23.30	62.23	1.48
	Emmetropia	23.38	62.02	1.84
3	— 3.0	24.27	61.81	1.55
	Emmetropia	24.26	61.19	2.43
4	— 3.0	25.06	59.03	1.22
	Emmetropia	25.09	58.21	2.14

placement of the posterior principal plane influences refraction in the same way as increased length of axis. A change of 1 mm in the length of axis causes an average change of refraction of 3.0 D. These figures are in complete conformity with data obtained in my 4 cases concerning the relation between the degree of myopia and the position of the posterior principal plane.

To what group of refractive anomalies should ametropia caused by various positions of the posterior principal plane belong? The answer is based on the classification of anomalies of refraction which I suggested in one of my earlier studies on refraction.<sup>1</sup>

All the spherical anomalies of refraction may be divided in four groups. This classification is based on changes in optical elements in 60 em-

metropic eyes, established by means of ophthalmophakometric measurements

1 Axial ametropia refractive power of the eye within the limits for emmetropic eyes, rather considerable values for length of axis, as observed with emmetropia

2 Refractive ametropia length of axis within values observed in emmetropic eyes, rather considerable values of refractive power, as observed with emmetropia

3 Mixed ametropia length of axis and refractive power greater or less than values observed in emmetropic eyes

4 Combination ametropia values for length of axis and for refractive power not beyond values obtained for emmetropic eyes, but their interrelation differing from that observed in normal eyes

Ophthalmophakometric measurements on 60 emmetropic eyes showed that the refractive power of emmetropic eyes varies from 52.59 to 64.12 mm, and the length of axis, from 22.42 to 27.30 mm. It is obvious that the cases of ametropia belong to neither of these groups of anomalies. They seem to be closer to the group of combination ametropias because in this type refractive power and length of axis remain within the values observed in emmetropic eyes.

However, these cases of ametropia differ from combination ametropia in the following features. Length of axis and refractive power in ametropia are similar to those in emmetropia but interrelations of these optical elements are different. In ametropia due to the position of the posterior principal plane, values for the length of axis and for refractive power are not only within the limits of those occurring in emmetropia, but the interrelations of these optical elements are also identical in the two conditions. In these cases, ametropia is caused by the position of the posterior principal plane. Thus these cases present a new kind of ametropia. The difference between this new kind of ametropia and combination ametropia is explained in table 5, in which cases of combination ametropia and cases of ametropia induced by the position of the posterior principal plane are compared.

Variation in the position of the posterior principal plane can cause not only ametropia but various degrees of refractive anomalies. Our material contains 8 illustrative cases. Data given in table 4 show that differences in refraction produced by the position of the posterior principal plane never exceeds 3.0 D. The fact that ametropia induced by the position of the posterior principal plane reaches but a small value can be explained by the insignificant variation of the

posterior principal plane (1.06 to 2.51 mm). Much greater is the variation in refractive power and length of axis. As seen from the results of my investigations, the values for refractive power based on data obtained by measurement of 275 eyes varied from 52.59 to 66.88 mm, and values for length of axis, from 20.75 to 38.08 mm. We have noted that values for ametropia belonging to other groups reached higher degrees. Thus, axial ametropia reached +10.0 D in cases of hypermetropia and -25.0 D in cases of myopia, refractive ametropia reached -13.0 D, mixed ametropia, +2.5 D in cases of hypermetropia and -15.0 D in cases of myopia, and, finally, combination ametropia reached +5.0 in cases of hypermetropia and -10.0 D in cases of myopia.

After we had established the significance of variability of the position of the posterior prin-

TABLE 5—Combination Ametropia and Ametropia Caused by Position of Posterior Principal Plane

	No	Change in Refraction	Length of Axis, Mm	Refractive Power of Eyes, Mm	Position of Posterior Principal Plane Mm
Combination ametropia	1	+4.0	23.52	56.77	1.54
		Emmetropia	23.50	60.76	1.57
		Emmetropia	25.02	56.81	1.50
	2	-3.0	24.27	61.61	1.55
		Emmetropia	24.29	58.61	1.49
		Emmetropia	23.46	61.50	1.74
Ametropia caused by position of posterior principal plane	3	-1.0	23.42	62.20	1.59
		Emmetropia	23.49	62.10	1.93
	4	-3.0	24.27	61.81	1.55
		Emmetropia	24.26	61.19	2.43

cipal plane for refraction, it was necessary to consider anisometropia and isometropia from this point of view.

Our material contained 22 cases of anisometropia, with a difference in the refractive power of the two eyes of from 2.0 to 13.0 D. I established the optical basis of anisometropia in one of my earlier works by considering the condition of the visual apparatus in these cases. Anisometropia can be divided in three types: (1) axial anisometropia, a difference in the refraction of the two eyes caused by a difference in the length of axis, (2) refractive anisometropia, a difference in refraction of the two eyes caused by a difference in refractive power, and (3) anisometropia of mixed origin, a difference in refraction of the two eyes caused by differences in the length of axis and in refractive power.

From the point of view of the position of the posterior principal plane in the two eyes, all the cases of anisometropia can be divided in

three groups (1) Insignificant difference in the position of the posterior principal plane, of less than 0.1 mm, (2) middle value of difference in position of the posterior principal plane, from 0.1 to 0.5 mm, (3) difference in position of the posterior principal plane considerably greater than 0.5 mm. The respective degrees of anisometropia in these groups are as follows: group 1, from 2.0 to 7.5 mm; group 2, from 2.0 to 13.0 mm; group 3, from 2.0 to 4.5 mm. Consequently, high and low degree of anisometropia may be encountered with considerable, as well as with insignificant, differences in the position of the posterior principal plane in the two eyes. Therefore, the difference in the position of the posterior principal plane is of no importance in the genesis of anisometropia.

In 7 cases of isometropia, changes in the position of the posterior principal plane in the two eyes were insignificant. They vary from 0.04 to 0.25 mm, and only in 1 of these cases was the difference greater than 0.2 mm.

#### CONCLUSIONS

1 The position of the posterior principal plane in the optical visual system is subject to great variation. In 275 eyes with refractive power of from +10.0 to -25.0 D, it changed within the limits of 1.06 to 2.51 mm, an average value of 1.63 mm.

2 The position of the posterior principal plane is the same with various types of refraction.

3 A positive correlation occurs between the position of the posterior principal plane and the refractive power of the eye and of the lens. The greater the refractive power of the eye and of the lens, the farther the posterior principal plane is situated from the cornea. The coefficient of correlation between the position of the posterior principal plane and the refractive power of the eye is +0.54. The length of axis has no effect on the position of the posterior principal plane.

4 A special kind of ametropia is to be noted, in which a refractive anomaly is caused by the position of the posterior principal plane in the optical vision system. This kind of refractive anomaly is seldom encountered, only 4 cases out of 215, or 1.85 per cent, being encountered. Ametropia caused by the position of the posterior principal plane reaches only a slight degree (3.0), the relatively small variability of the posterior principal plane accounts for this fact.

5 The position of the posterior principal plane may be the cause not only of ametropia but of a difference in the degree of refractive anomalies, without reaching any considerable value owing to the same cause.

6 Changes in the position of the posterior principal plane are of no importance whatever for the genesis of anisometropia.

7 Changes in the position of the posterior principal planes in both eyes are inconsiderable in isometropia.

# Clinical Notes

## MARFAN'S SYNDROME WITH UNUSUAL COMPLICATIONS

### Report of a Case

JAMES L. MCGRAW, M.D., NEW YORK

Since Maitan, in 1896, first described the case of a young girl with the symptom complex of arachnodactyly and ectopia lentis, there has appeared in the literature a sufficient number of similar cases so that this syndrome can no longer be placed among the rare diseases. The reported number of typical and atypical cases is now well above 200.

The present case is a typical instance of Marfan's syndrome, with some unusual complications.

The patient is the sixth child of normal, healthy parents and grandparents. The first child, a boy, died at the age of 6 years in a home for mentally deficient children. He was mentally defective, and was subject to convulsive seizures. He was said to have an enlarged thymus gland. There was no known ocular disease. The second child, a boy, died at the age of 15 months, after a renal infection. This child was believed to have been normal in all respects. The third and fourth children are normal, healthy girls, aged 17 and 14 years. The fifth child, a girl, died at the age of 6½ years. This child was mentally retarded and had ectopia lentis and a double ninth rib on the right side. The child died, of unknown cause, in a school for mentally deficient children. The sixth child, the subject of this report, is a 6 year old girl, born at term after a normal, spontaneous delivery, prior to which the mother had an uneventful gestation. The child's development was slow. She spoke a few monosyllables at 15 months but did not talk until she was 3½ years of age. She stood at 16 months and walked at 2 years. The gait was always clumsy, and there appeared to be exaggeration of associated movements. The child was too retarded mentally to attend school. The parents noticed that vision had never been good, as the child was unable to recognize people or objects unless within very close range. A few weeks before the child's admission to the hospital the mother first noted what she described as a bubble or a drop of oil in the pupil of the right eye, which was present only at irregular times.

Examination revealed a tall, thin girl, with an apathetic, pained expression. She was 48 inches (121 cm) tall and weighed 46 pounds (20.9 Kg). The findings on general physical examination were essentially without significance except for prominent ears, a long, thin flat chest, winging of the scapulas, slight curvature of the spine, and abnormally long, spider-like hands and feet. The ophthalmic examination was diffi-

cult because of the patient's inability to cooperate. Visual acuity was not determined. The anterior chamber of the right eye was very deep, the pupil irregular and the iris tremulous. The lens was completely dislocated into the vitreous and was seen lying inferiorly. At irregular intervals the lens spontaneously luxated into the anterior chamber for short periods of time and then moved back into the vitreous. The results of examination of the fundus and estimation of tension with the fingers were normal. The anterior chamber of the left eye was shallow, the pupil small and eccentric and the lens partially subluxated downward and inward. Tension seemed elevated on palpation, and the fundus was not well seen. The pupils responded poorly to mydriatics. With the patient under general anesthesia, the tension in the right eye with the lens at the time in the anterior chamber was 23 mm and that in the left eye was 45 mm of mercury, as measured with the Schiøtz tonometer. An attempt was made to keep the lens of the right eye trapped in the anterior chamber by constricting the iris behind it with miotics, as an aid in the extraction of the lens. However, after section the pupil dilated, the lens dropped into the vitreous, and a complete iridectomy and loop extraction were done. After operation, the temporal pillar of the iris became incarcerated in the wound but did not prolapse. The postoperative course was otherwise uneventful.

Three weeks later, the lens of the left eye was removed by loop extraction after complete iridectomy. The postoperative course in this eye was uneventful. The lenses removed from both eyes were almost completely spherical.

After operation, retinoscopic examination revealed a refractive error of +9.00 sph bilaterally and glasses were prescribed, which gave vision of approximately 20/70 in each eye. The tension in both eyes was normal to palpation, and the fundi were seen to be normal.

Seven months after extraction of the lens of the right eye, a cyst developed in the anterior chamber on the temporal pillar of the iris. The cyst grew rapidly and within one month half filled the anterior chamber and caused a rise in tension in the eye to 40 mm of mercury (Schiøtz). The tension in the left eye was 23 mm. The child was readmitted to the hospital, and a needle was introduced into the cyst at the limbus. The fluid content of the cyst was evacuated and the cyst flushed several times with a 3.5 per cent solution of iodine. The iodine was withdrawn, the cyst collapsed, and the needle was removed. The eye remained slightly irritable for about two weeks after this procedure, but since that time has been white and quiet and the tension normal to palpation. Although suffi-

Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, April 16, 1945.

cient time has not elapsed to permit a report on the final outcome, there has been no evidence of recurrence of the cyst after six weeks

The salient features in this case are as follows

1 This case is a typical instance of Marfan's syndrome, occurring in a family in which 3 of 6 children were mentally deficient, and 1 of the 3 showed other congenital defects including ectopia lentis. In this case the usual features of arachnodactyly were present—ectopia lentis, apathetic expression, prominent ears, thin, flat chest, winging of the scapulas, and spinal curvature

2 The tension was elevated in the eye with partial dislocation of the lens but not in the eye with complete dislocation despite the presence of the lens in the anterior chamber at times

3 A cyst developed in the anterior chamber of the right eye seven months after extraction of the lens, causing a rise in tension in that eye

4 The method chosen for treatment of the cyst in the anterior chamber was ablation with iodine. The treatment was well tolerated and to date appears to have been successful

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## MODIFICATION OF A BLOOD PRESSURE APPARATUS FOR USE BY THE BLIND

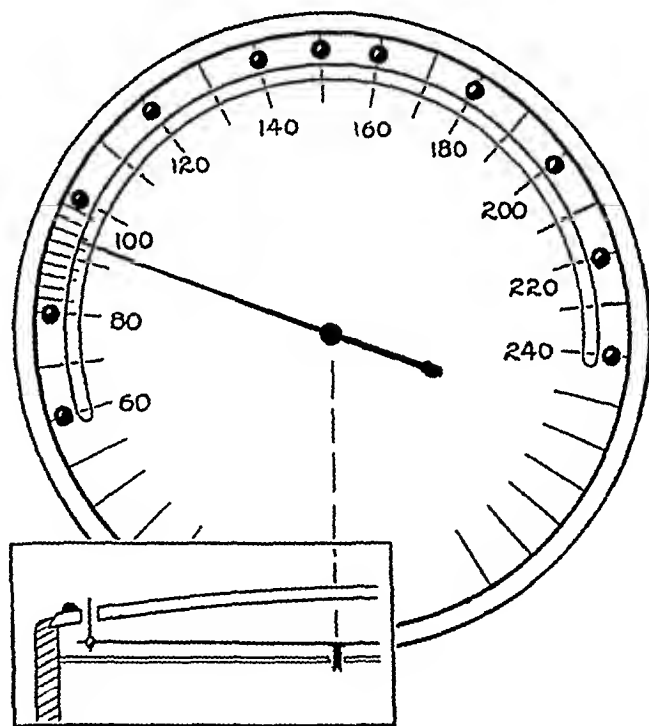
O. H. PERRY PEPPER, M.D., PHILADELPHIA

Recording the blood pressure is one of the steps in physical examination which is impossible for the blind physician with any of the usual types of sphygmomanometer. By a simple modification of the Tycos spring sphygmomanometer the procedure becomes easy after a little practice, with a range of error not exceeding 10 mm. of mercury.

All that is necessary to make it possible for a blind physician to read the gage is to cement a plastic fiber bristle at right angles to the outer third of the needle in such fashion that the tip of the bristle projects about one sixteenth of an inch (0.16 cm.) through a narrow slit cut through the plastic crystal covering the dial. The slit is circular in course and extends throughout the range of the scale. Small braille dots are attached to the crystal at points corresponding to the numbers of the scale, larger dots can be placed to correspond with readings of 100, 150 and 200 to orient the examiner's finger. (See illustration.)

This device was developed by J. O. Kleber of the American Foundation for the Blind as a result of a request to this Foundation. The apparatus has been used with success within its margin of error by the blind physician for whom it was devised. It is true that there are not many blind physicians in practice, but unfortunately there may be more as a result of war injuries. It seems proper, therefore, to draw

this device to the attention of the medical profession and to state that Mr. Kleber believes the use of this type of modification could be adapted to other gages and meters, enabling blind per-



Blood pressure apparatus for use by the blind

sons to read them by touch. The thanks of the medical profession are certainly due to Mr. Kleber for his interest and help.



# Ophthalmologic Reviews

EDITED BY DR FRANCIS HEED ADLER

## HERPES ZOSTER OPHTHALMICUS

REPORT OF CASES AND REVIEW OF LITERATURE

AMBROSE EARL EDGERTON, M D

SAN FRANCISCO

*(Concluded from page 62)*

### EPIDEMIC AND SYMPTOMATIC TYPES

Two main types of herpes zoster can be differentiated—the epidemic type, sometimes called primary, specific, idiopathic or true herpes zoster, and the symptomatic type, often called a secondary, nonspecific or zosteriform eruption. The last term was suggested by Darier in 1923, and by Teague, Goodpasture and Lipschutz, in 1924.

#### EPIDEMIC TYPE

True zoster is contagious and bears a resemblance to varicella, encephalitis and anterior poliomyelitis. An attack usually conveys immunity, and, like other exanthems, recurrence is unusual. It presents many symptoms commonly observed with eruptive febrile diseases, such as malaise, digestive disturbances and fever, which usually subside with the appearance of the eruption. True zoster runs a definite course, is not related to other disease and often appears in epidemics. Von Hoffmann, in 1879, reported one of the first epidemics of ophthalmic zoster, of 24 cases with ocular complications, during an epidemic of zoster.

#### SYMPTOMATIC TYPE

The symptomatic type of herpes zoster is associated with various diseases or complications of other disorders or may follow trauma or intoxication. Symptomatic zoster has a very different history from that of the epidemic type. The eruption is due not to a virus but to secondary involvement of the nerve or posterior root ganglion in the course of other disease. This eruption is unaccompanied with fever, runs a chronic course, subsides and may recur, depending on the cause. The eruption clears rapidly, without deep scarring and pigmentation, and is preceded by severe pain for several days, or even weeks. The histologic changes are the same as those in true zoster—small round cell infiltrations, hemorrhagic extravasation, destruction of ganglion cells

and inflammation of nerve sheaths. At the onset the symptoms are frequently the same as those of true zoster as far as the ophthalmic form is concerned. The evolution and termination are variable.

In the literature, symptomatic zoster is attributed to the most diverse etiologic factors, ranging from acute infection to various kinds of trauma, errors of refraction and even severe mental strain and emotion. Besnier related the case of a student in whom the disease developed while he was studying a case. Among etiologic factors are syphilis, tuberculosis, acute or chronic infections, metabolic diseases, chronic poisoning, multiple sclerosis, malaria, leukemia, degenerative processes, atmospheric conditions, exposure to wind and rain, subarachnoid hemorrhage and trauma. Numerous cases have been reported in which the eruption followed lesions of the orbit, pontile tumors, fracture of the base of the skull or spine, extraction of teeth, cataract operations, retrogasserian neurotomy and various kinds of wounds.

The symptomatic type is associated with toxic, inflammatory or neoplastic damage involving the fifth nerve, the gasserian ganglion or fibers that constitute the central connections of the nerve. Cases have been reported in which the causative factor was arsenic, mercury, bismuth, iodides or carbon dioxide poisoning, and the disease has followed pneumonia, meningitis, influenza, diabetes and gout. In many cases the condition bears a distinct relation to diseases of the general nervous system and degenerative processes.

The process may extend to the fibers of the posterior root and may extend into the gray matter, affecting chiefly the posterior horn, the anterior horns may also be involved. Duke-Elder stated that some of the lesions which develop may be due to the primary central lesion, and not to involvement of the ganglion, and that the primary cause may be latent at the time of

the eruption and the secondary nature of the zoster may be diagnosed some time after it has subsided

Symptomatic zoster is likely to occur when the first sensory neuron is damaged. Once the virus has entered the sensory neuron, it proceeds peripherally toward the skin and centrally toward the neuraxis. R. T. Brain suggested that the susceptibility of the first sensory neuron in adults may be due to its possessing a tissue immunity more feeble than that of other parts of the body or to its immunity being lowered by a preceding lesion.

Chronic inflammatory disease predisposes to herpes zoster. This process within an internal organ has been explained by van der Scheer, in 1913, and by Nyáry, in 1921, who in his summary stated that a morbid process within an internal organ irritates centripetal sympathetic fibers. The irritation is transmitted by way of the ramus communicans of the sympathetic trunk to a spinal ganglion. If such centripetal irritation is of sufficient intensity it may go on to the cerebrum and cause pain. If not of sufficient intensity, a state of irritability persists in the ganglion, which may spread to other centripetal sensory fibers from the skin, thus producing hyperalgesia of Head's area. Such a prolonged state of irritability of a spinal ganglion produces physiochemical changes within the ganglion cells and sets up a local predisposition to infection with the herpes zoster virus or with other pathogenic organisms.

## ETIOLOGIC FACTORS

### INJURY

Injury probably serves as an exciting factor. Many cases have been reported in which the infection developed in the region which had suffered the injury, with or without a lesion of the skin. The eruption developed soon or in the course of a few weeks.

Many investigators attribute zoster to a virus which first affects the skin and then, by an ascending process, reaches the nervous system. They believe that the trauma acts by diminishing locally the resistance of the organism to a zoster virus, preexistent in the region, and thus its resistance to a virus which it normally harbors is reduced. In many cases in the literature the cause is given as an injury to the head or eyelid, as described by Hofer, Terrien, Hildeheimer, Gauchard and Bernard, and Flemming. Charcot, as early as 1859, published his account of a case of recurring herpes zoster following

a gunshot wound. Herpes zoster has followed peripheral nerve trauma, as reported by Moore, Knowles, Kinnicutt, Coursserant, de Salterain, Duméry, Terrien and Bayer, and central trauma, as reported by Gunn. Zoster has followed surgical operations on the trigeminal for neuralgia, due to injury of the dorsal root ganglions. Also, infiltration of the ganglions by tumor or by a leukemic process has caused the eruption. Apparently, anything which may bring about an irritable or inflamed gasserian ganglion, spinal ganglion, nerve tract or peripheral branches may be responsible for the eruption. Knowles stated, however, that in cases of traumatic origin the ganglions are not involved but the peripheral nerves alone are the seat of the pathologic changes. Caspar, in 1906, cited a case of herpes zoster ophthalmicus in a youth of 18 years in which the eruption developed four days after a tattooing operation on the cornea. Schiffer reported a case of ophthalmic zoster in a patient with a melanotic sarcoma of the sphenoid bone. In this case the oculomotor paralysis preceded the eruption by several weeks. Landis described a case in a man, with chronic frontal sinusitis and ethmoiditis. A radical operation on the frontal sinus revealed pus and a hyperplastic mucous membrane undergoing polypoid generation. This was removed, and an opening was made into the nose. On the second day the eruption began to disappear, and on the twelfth day little was seen of the vesicles. Schiffer stated the belief that the disease was due to a peripheral reflex irritation from chronic frontal sinusitis. Fésus reported a similar case in 1936. Fourestier, in 1939, described a case of zoster in a man following an operation on the lung for tuberculosis. During the operation the anesthesiologist injured the right malar region with the mask. Nine days later, a typical eruption of zoster developed, involving the right upper lid and the right side of the nose, and soon became bilateral. Snell, in 1896, reported a case of zoster that followed an operation for removal of cataract. Ammann mentioned 9 cases in which injury was followed by typical herpes zoster. He stated the belief that the virus of herpes simplex was identical with that of herpes zoster and that each disease could be caused by injury. Lloyd stated that any or all of the dendritic group might follow an injury to the eye, allowing the virus to enter the deeper tissues and then to travel along the nerve sheaths to the ganglion. Nicolau and Dragenescu, in 1936, reported a case in which the disease developed five days after an injury to the left

frontal and temporal regions. Involvement of the cornea was complicated with complete ophthalmoplegia. They stated the belief that a neurotropic virus passed from the skin over the sensory nerves to the motor nerves. Raecke, in 1910, mentioned a case of herpes zoster in a man aged 64 who was injured in the left eye, the injury was followed in ten days by violent ophthalmic zoster. He stated the belief that the mechanical irritation called the inflammation of the nerve into being. Terlinck, in 1928, reported a case of zoster in a woman aged 25 who had had an injection of alcohol into the gasserian ganglion for treatment of neuralgia. Total anesthesia of the first and second branches of the fifth nerve developed. One month later a typical ophthalmic zoster appeared, involving these two branches of the fifth nerve. Raecke stated the belief that the permeability of the ganglion cells was modified by the injection of alcohol, and thus the unknown herpetic virus penetrated the ganglion cells, ascended along the lymph tracts to the sensory neurons and produced the eruption. Grandi, in 1937, described a case of zoster in a man who was struck in the right eye while emptying a bag of fertilizer. Two days later he exhibited photophobia and conjunctival hyperemia. On the fifth day the cutaneous picture of herpes zoster appeared over the affected region, with edema of the lids and severe pain. One week later there was deep infiltration of the cornea, with posterior corneal deposits and iritis. The relation of trauma is explained on the assumption that there was loss of corneal tissue whereby the herpetic virus was enabled to localize itself in the corneal parenchyma. Bariaux, Assale and Bastouil, in 1935, described a case in a man aged 25 who was struck in the right orbital region with a football. Eight days later he experienced severe pains in the right orbit with nausea and vomiting. Symptoms of meningeal depression developed, and he was hospitalized. There was severe cephalalgia in the right fronto-orbital region. Ptosis of the right upper lid was noted, with keratoconjunctival injection. Soon there developed a typical ophthalmic zoster, with mydriasis and keratitis. While the virus of herpes zoster is localized in the ganglions of the posterior roots and its lesions spread to the cord and the nuclei of origin of the sensory nerves of the cerebral area corresponding to the posterior horn cells of the cord, the authors believe that trauma involving the vicinity of the usual site of election of zosteric manifestations may, by reactivation of the virus existent in the latter state in the organism, provoke the occurrence of zoster.

#### SYPHILIS

Numerous cases of herpes zoster have been reported in association with syphilis of the central nervous system. Syphilis has been given as a cause in cases reported by Schaller, Proust, Head and Campbell, Allbutt and Rolleston, Filatov, Busfield, Doggart, Picault, Clark, Rollet and Colrat, Ebaugh and Jefferson, Townes, Boner, Osterholt, Rosenmayer, Weill and Reys, Lagenhan, and Murzin. Dujardin found 9 cases of herpes zoster in 1,200 cases of syphilis. Morax commented on the frequency of syphilis in patients with zoster. Brown and Dujardin, in 1919, stated that the frequency of occurrence of herpes zoster is four times as great in syphilitic as in nonsyphilitic persons. Schaller concluded that symptomatic herpes zoster occurred with comparative frequency in cases of syphilis of the central nervous system. Head and Campbell, of 21 cases of zoster, found positive evidence of syphilis in 14. However, the zoster may be due to the arsenical treatment. The slight meningeal irritation in syphilis may open the road to infection with the virus of herpes zoster, and arsenical treatment, or inefficient arsenical treatment, may predispose to herpes zoster. Valiere-Vialeix, in 1931, reported a case of a female with parenchymatous keratitis following ophthalmic zoster. The patient had a positive Wassermann reaction, and after antisymphilitic treatment the vesicles rapidly disappeared. Lepine, Christy and Feuillade, in 1932, cited a case of a man of 32 with corneal ulceration and violent neuralgia. In this case the herpes zoster occurred two months after right hemiplegia. They stated the belief that in this case there was a pathogenic correlation. The signs of hemiplegia and zoster retrogressed rapidly. They thought that the zoster was due to an infectious lesion, localized in the protuberance involving the root of the right trigeminal nerve. Renard described a case in a woman of 31 years. The corneal microscope revealed deposits on the posterior surface of the cornea and exudate in the pupillary area. The Wassermann reaction was positive. Treatment was instituted, and all symptoms of zoster disappeared. Three months later the left pupil was dilated and immobile. There was no reaction to light, in convergence or consensually. There was slight contraction in accommodation. The paralysis in this case developed long after disappearance of all symptoms of herpes zoster. Renard believed that a primary attack of meningeal syphilis doubtless involved the gasserian ganglion and produced the zoster and the paralysis of the iris. It is difficult to decide whether

the pupillary paralysis is due to herpes zoster or to infection with *Treponema* in cases in which syphilis exists

#### ENCEPHALITIS

Herpes zoster has been found associated with evidence of involvement of brain tissue. Symptomatic zoster may follow a lesion of the nervous system, and in some cases it is questionable whether the zoster is secondary to encephalitis of different origin or whether the encephalitis is due to the zoster. Most investigators believe that encephalitis may damage the first sensory neuron and lead to an outbreak of zoster or that the virus may cause the encephalitis by extension. Netter reported that in 1 per cent of cases encephalitis was accompanied with supra-orbital herpes zoster followed by paresthesia of the skin. Schiff and Brain reached the conclusion that there was a group of cases in which an extension of zoster infection had produced the clinical picture of encephalitis. Bedson and Bland supported this view. Tilney and Howe, in 1920, described a case of encephalitis characterized by weakness, blurred vision and diplopia. After three weeks a typical herpes zoster developed along the course of the third nerve. Similar cases have been reported by Wilson, Netter and Annand.

#### ARSENIC POISONING

Numerous cases of ophthalmic zoster following arsenical treatment have been reported. Arsenic may predispose to the disease in some persons, but it is possible that the drug may cause irritation of the gasserian ganglion, and this has been observed at autopsy. Hutchinson reported the first case of ophthalmic zoster due to arsenical poisoning in 1869. Other cases have been reported by Head and Campbell, Powell, Cohn, Gerson, Pearce, Wilbrand and Saenger, Pergola, Weber and Broadbent. Pearce, in 1930, described a case in a girl of 7 years, with chorea, who was taking an arsenical preparation in treatment. When all the symptoms of chorea had disappeared, there developed typical ophthalmic zoster, probably the result of arsenical poisoning of the ganglion. Arnstein, in 1922, mentioned 6 cases of zoster following arsphenamine treatment in 2,211 cases of disease of the skin. He considered the eruption in these cases to be some form of the Herxheimer reaction. It is almost impossible to determine whether the zoster is due to the treatment or to the disease from which the patient is suffering. Palazzo in 1921, described a case in

a man of 42 who was under treatment for acute pulpitis of the second lower right molar tooth. The carious cavity was cleansed, and arsenical treatment was applied for cauterization of the pulp. A few hours later the patient complained of severe pain over the entire right half of the head, particularly in the fronto-orbital region. Shortly after typical ophthalmic zoster developed. Arsenical medication applied to the pulp may produce an irritation capable of manifesting itself reflexly in the form of zoster and may be an evident expression of arsenical idiosyncrasy. Until a few years ago, the possible occurrence of odontogenic zoster was not considered, but numerous instances of the appearance of zosteric eruptions in consequence of dental irritation have been recorded in which there had been no arsenical medication. Potassium iodide and bismuth preparations have been reported as exciting or supplemental causes of zoster by Griffith, Netter and Urbain, Jacquet and others. Many cases of herpes zoster have been described as following carbon dioxide poisoning. Severe inflammatory changes have been observed in the ganglion in cases reported by Cohn, Kozlowski, Sattler and Kaposi.

#### ACUTE DISEASES

Sicard, in 1905, reported a case of a boy of 12 years with bilateral parotiditis, due to mumps. A few days later zoster developed, localized over the left half of the face, in the frontal, supra-orbital and superior palpebral regions, with symptoms of meningitis. These symptoms rapidly disappeared, and recovery followed. In this case the first and second branches of the trigeminal were affected. The zoster was attributed to the cutaneous trophic disturbance produced by extension of the meningeal process to the gasserian ganglion. Accordingly, in this case the trigeminal zoster in the course of mumps provided evidence apparently of a meningeal process at the base of the cranium. Galezowski mentioned a case of zoster which occurred during the course of pneumonia. Bane, in 1916, described a case of zoster in a man following an attack of grip, and Schaffer published a case in which the condition followed bronchopneumonia. Many cases have been reported in which the disease was a complication of leukemia, as cited by Freund, Glaubersohn and Márquez. Diabetes has been ascribed as a cause of zoster by Atkinson. Schiffer, cited by Jessop, mentioned a case in which a sarcoma of the sphenoid bone was found, and Charcot mentioned a case of zoster occurring in the course of an orbital

tumor Lucic, in 1930, described a case of the disease in a man, with corneal vesicles. Eight months later, after a submucous resection, the corneal symptoms reappeared, and hospitalization was necessary, with eventual loss of the eye. Chance stated the belief that sinus disease has a close relation to ophthalmic zoster as a contributing cause, and that filaments of nerves supplying the sinuses are affected in their passage through the sinuses and thus transmit infections to the nerve branch. Carter told of a case of zoster following lumbar puncture. It was thought to be due to traumatic irritation transmitted to the dorsal root ganglion. Coppez described a case, in which one year after the attack, the eye became inflamed and painful at each menstrual period.

#### CHICKENPOX

Much clinical evidence has been presented to associate herpes zoster and chickenpox. Many writers have drawn attention to this close relationship, among them von Bokay, McEwen, Jacobi, Bedson and Bland. Work on herpes zoster and varicella is extensive, and it has been demonstrated on clinical and experimental grounds that there is a definite etiologic relationship.

Netter and Urbain claimed on the basis of deviation of complement that the virus of herpes zoster is identical with that of varicella. Amies found elementary bodies in the serum of patients with zoster and varicella which were morphologically similar. Many investigators, among them Brain, Paschen and Pickard, have claimed that the antibodies are identical. The histologic characteristics of the vesicle are the same in chickenpox as in herpes zoster, and it has been possible to observe evidences of cross contamination, while the fixation reaction is the same with both antigens. However, varicella is inoculable, and herpes zoster is not, the hematologic formulas are not the same, neither is the spinal fluid changed in varicella, while it is altered in zoster. Animal experimentation to prove the similarity of the viruses in the two diseases, however, has not been successful. The investigations of Netter and Urbain showed that there were antibodies in the blood of the patient suffering from herpes zoster. Deviation of the complement occurred when the crusts from the vesicles of zoster or varicella were used as antigen against the blood serum of patients with zoster, and the same results were found with the antigens and the serum of patients with chickenpox. In 1926, these authors reported

100 cases of herpes zoster, in 93 of which deviation of complement occurred. De Lange, in 1923, claimed to have demonstrated antibodies in the blood of a patient with zoster. Bedson and Bland substantiated these claims. The relationship of the two diseases is strengthened by the interchangeable fixation reactions and the transmission of zoster by patients with varicella and the production of chickenpox by inoculation with the zoster virus. Pickard claimed that the virus causing varicella and zoster has two phases, which are transmutable. The zoster phase has its seat in the posterior root ganglion, from which the infection may spread locally, involving the gasserian ganglion, and extend along the sensory nerves to fibrous tissue covered with epithelium, where it reverts to the varicella stage.

In view of the number of cases of herpes zoster following varicella and of cases of varicella following zoster, either disease may be the starting point for an epidemic of either type of disease. Von Bokay, in 1898, was the first to call attention to the relationship existing between epidemics of varicella and of herpes zoster and reported that most cases of herpes zoster occurred one month after epidemics of varicella had reached their height. Such a relation has been emphasized by Netter and Urbain, Brain, Paschen, Amies and Pickard. Levine stated the belief that epidemic zoster and epidemic varicella were produced by modified strains of the same parent virus, which would explain the interchangeable fixation reactions in the two diseases and the high protection each disease gives against recurrence. He reported 6 cases of zoster following exposure to varicella and 3 cases of varicella following herpes zoster. Low considered that the two diseases have identical viruses and differ only in their mode of attack.

Some investigators believe that the virus which causes herpes zoster in the adult may cause varicella in the child. This belief is based on the development of zoster in adults caring for patients with varicella, and many instances have been cited in which there has been the curious incidence of varicella in children after an adult member of the family had herpes zoster. Le Feuvre, in 1917, stated that under certain conditions herpes zoster may be the starting point of an epidemic of varicella. He reported 41 cases of varicella following exposure to zoster. The interval between the zoster and the varicella and between the varicella and the zoster averaged fourteen days. Netter collected 174 cases of varicella following exposure to zoster. The incubation period varied from seven to twenty-



four days Renard and Halbron, Sayeys, Pado-vani, Busfield, Roxburgh, Ardoun, Low, Paton, Viallefont, von Bókay, Roberts and Quick have described such cases Hill found 9 cases of varicella following zoster and 1 case of zoster following chickenpox Netter and Ernoul, in 1934, reported an interesting case During an operation for evisceration of the globe following purulent dissolution of the cornea in the course of ophthalmic zoster, a physician pricked himself in the hand Twenty-six days later there was a typical eruption of zoster in the region of the extension of the left median nerve Three weeks later his two children became ill with varicella It was presumed that the virus, by following the nerves, had penetrated into the intervertebral ganglions and that it must have traversed the same route in an opposite direction in order to produce a typical herpes zoster in the corresponding cutaneous region

It is less frequent for zoster to follow exposure to varicella, although Netter collected 25 cases of such an occurrence in 1928 Thus, zoster may be followed by zoster in one person and by varicella in others and the same is true of varicella, or a person may have both diseases at the same time Almost all the patients with varicella from exposure to zoster have been children and the patients with zoster from exposure to varicella have been adults

Herpes zoster and varicella have occurred at the same time in the same person A two phase virus might produce this condition, each phase being transmuted into the other Von Bókay recorded 29 cases in which zoster and varicella occurred simultaneously Many similar cases have been recorded by Ormsby, Pollitzer, Schamberg, Stelwagon, Corlett, Genet, Barling and Cahill, Le Feuvre, Hunter, J B Harris, Schiff and Brain, Watt, Davenport, Zander-Olsson, Barraux and associates and Guillian and associates Although the simultaneous occurrence of zoster and varicella has often been reported, the relation of the two disorders has thus far not been explained The histologic appearance of the vesicles in the two diseases is similar Perivascular infiltrates are found around the intervertebral ganglions in both diseases However, there is yet no evidence to show conclusively that varicella and zoster possess the same cause and are due to an identical virus Brooks, in 1931, reported the case of a man aged 70 who was admitted to the hospital complaining of persistent hiccup There was a history of malaise for two weeks previously, then hiccup began and had been persistent for three weeks

Shortly after being hospitalized, he broke out with typical varicella and a profuse zoster rash This chain of events seems related to a virus infection and illustrates the close relationship of zoster, varicella and encephalitis and between encephalitis and hiccups Cornil and Blanc, Rokitskaya, and Shelmire and Shelmire have reported similar cases

Low suggested that varicella is an infection of the blood while in zoster the virus reaches the posterior root from the spinal fluid, to which it gains access through the nose He stated that they differ in their manner of attack, zoster spreading by way of the lymphatics and varicella by way of the blood

Paton held a similar view and expressed the belief that the two diseases might be due to the same virus, differing only in intensity Stern asserted that the virus which causes zoster might revert to the varicella phase, after extending along the sensory nerves from the ganglion, when it reached the cells of ectodermal origin Barker, in 1939, reported 3 cases of herpes zoster ophthalmicus in males, in which there was a generalized vesicular eruption on the trunk and extremities, clinically similar to varicella The latter, he believed, however, to be an extension of the zoster itself or to be due to a dissemination of the virus The generalized eruption disappeared in ten days, and the original zoster lesions followed the usual course Kundratitz claimed to have produced varicella by inoculation with zoster vesicles In 1925 he was able to prove that the virus of varicella and the virus of herpes zoster are closely related, by immunizing children against varicella by means of the inoculation of material from patients with zoster In 1927 he reported 26 successful attempts This inoculation was also successfully made by Netter and others A successful inoculation protected against subsequent infection with zoster and also against varicella Lipschutz, in 1921, was able to inoculate rabbits with herpes zoster by rubbing vesicular fluid into their scarified corneas, with resulting opacities Histologic study showed hypertrophied and swollen connective tissue cells, in the nuclei of the epithelial cells and in the tissue cells were found intranuclear inclusion bodies Cole and Kuttner, in 1925, in a series of cases, were unable to confirm the observations of Lipschutz regarding the experimental production of specific lesions in the corneas of rabbits It is very questionable whether herpes zoster can be so transmitted Many other investigators, namely, Kraupa, Baum, Lowenstein, Netter and Urbain, and Doerr, reported entirely



negative results from the inoculation of the vesicles of herpes zoster into rabbit corneas. Some investigators have claimed that the etiologic agents of varicella and of zoster are the same while Cole and Kuttner stated the belief that zoster is due to a modified virus of herpes simplex. Tyzzer, and Teague, Goodpasture and Lipschutz claimed to have found intranuclear inclusion bodies in the epithelial cells of the cutaneous lesions of all three diseases.

### HERPES SIMPLEX

Herpes zoster is thought by some investigators to be related to other disorders caused by a neurodermotropic virus, such as herpes simplex, although the latter does not produce immunization, is inoculable, exhibits no neural distribution and fails to show the fixation reaction of herpes zoster. The clinical manifestations of the two diseases are different, and the histologic lesions are not the same. Neuralgia does not precede the eruption. Herpes simplex lasts only a few days and is a local lesion, sensibility is not diminished, and the skin does not scar. The neuralgia pain is less severe and less persistent. Ocular tension is not reduced.

In recent years a vast amount of work has been done on the various manifestations of herpes of the cornea and herpes zoster. Buhne-mann, in 1937, stated that two diverse views are entertained concerning the identity of the viruses of herpes zoster and herpes simplex. One of these opinions is to the effect that the herpes neuralgias of zoster represent the form of herpes with an especially prominent neural component. The proponents of this theory affirm an etiologic relationship of the two pathologic agents, which, though they may differ morphologically, nevertheless produced the same specific injuries to the nerves. Adherents to the other opinion, while they admit the alleged identity of the viruses so far as it relates to the production of vesicular eruptions on the skin and of injuries to nerves, insist that these pathologic agents are essentially quite distinct. The latter hypothesis is now accepted by the majority of authors, who conclude that zoster is produced by a specific pathologic agent and that the virus is not identical with the virus of herpes simplex, although the pathologic pictures of the two conditions agree in some details.

At times there is confusion in diagnosis between herpes zoster and herpes simplex, especially when the vesicles of herpes simplex appear over the distribution of a nerve or when they recur. In some cases the cornea reveals approximately the same clinical picture with both herpes

zoster and herpes simplex, such as minor epithelial defects, superficial opacities, parenchymatous opacities, ulceration, and at times panophthalmitis, resulting from secondary infection.

Some authors have suggested that herpes zoster, herpes simplex, encephalitis and varicella are probably caused by the same virus. Many believe that a close relationship exists among the viruses producing anterior poliomyelitis, chronic epidemic encephalitis and herpes zoster because the pathologic changes that take place in the central nervous system are similar in the three diseases. The round cell infiltration of the gasserian ganglion in zoster, of the anterior horn cells in poliomyelitis and of the substantia nigra in encephalitis. The relationship of the herpetic virus to the virus of epidemic encephalitis is apparently so close that the majority of investigators unhesitatingly designate both etiologic agents by the general denomination of herpetic-encephalitic virus. Lloyd stated that the encephalitis following grip and the herpetic lesions following grip form the basis of the belief that the herpetic virus is the etiologic agent of encephalitis, multiple sclerosis, poliomyelitis and ascending paralysis. The histologic changes in the central nervous system in herpes simplex are similar to those in encephalitis, although inclusion bodies have not been found in the latter. Levaditi expressed the belief that the two diseases might be manifestations of infection with the same virus. Duke-Elder stated that herpes simplex was closely related to encephalitis but only doubtfully so to herpes zoster. Flexner produced anterior poliomyelitis in monkeys by infecting them with cultures obtained from vesicles of herpes zoster.

Many investigators believe that zoster is not caused by any specific organism and has a common etiologic agent with herpes simplex. The evidence that zoster may result from infection with the virus of herpes simplex rests on a small number of cases and needs further investigation. Luger and Landa claimed to have obtained the virus of herpes simplex from vesicles of zoster. Teague and Goodpasture stated that they had produced zoster-like lesions in the skin of rabbits by inoculation of the virus of herpes simplex. Grueter inoculated the cornea of rabbits with material from patients with zoster, and mild keratitis resulted. These investigators concluded that the reaction was specific and attributed it to the virus of herpes simplex of low virulence. They concluded that the two viruses were closely related, probably differing only in virulence. They stated that herpes simplex was a dermatotropic strain of the neurotropic zoster virus and that the two diseases were

different manifestations of the same entity. The consensus, however, is contrary to this conclusion. Androgé stated that the virus of herpes simplex was predominantly dermatropic, that is, the cutaneous lesions were more numerous than the neural lesions but that the contrary was true of zoster virus, which was predominantly neurotropic.

On the other hand, Lowenstem, in 1920, proved experimentally the difference between herpes simplex and herpes zoster. Zoster could not be transmitted to the cornea of rabbits, but all such attempts with herpes simplex were successful. Mariana was able to transfer various types of herpes simplex from one rabbit cornea to another, with changes in the nervous system, but in the case of herpes zoster he did not find changes either in the eye or in the nervous system. Lloyd claimed that the vesicles of zoster do not contain virus which can be transmitted to the corneas of rabbits but that the vesicles of herpes simplex do contain a transmissible virus.

The serum of patients convalescing from zoster gives complement fixation with the antigen preparations from zoster vesicles, while the serum of patients with herpes simplex shows no such properties. Although herpes zoster is always included among the diseases due to non-filtrable viruses, direct evidence in support of this view has not been produced. The work of Netter and Urbain, Bedson and Bland, Aitken and Brain, Kundratitz and Brussgaard indicates that the serum of patients with zoster contains a specific antibody the presence of which can be detected by complement fixation tests, using as antigen diluted fluid from the zoster vesicles or a suspension of the cutaneous crusts. According to the findings of these investigators, zoster may be regarded as an infection with a virus, which leaves evidence of itself, after the illness has passed, in the form of antibodies in the serum. Weizel reported a case of a patient who had received a transfusion of blood from a patient with herpes simplex and in three days had a typical eruption of herpes zoster on the cheek. Animal inoculation of material from these vesicles was unsuccessful. Injection of fluid from vesicles into the author's arm produced a papular eruption, which was not like any known exanthem.

#### PATHOLOGIC FEATURES

Von Baresprung, in 1861, attributed the disease to lesions of the posterior root ganglion and was the first to report on pathologic investigations. In 1865 Charcot and Catard noted injection of the capillaries and nerves in the gan-

glion. In 1870 Wagner and Weidner each noted changes in the ganglion and nerves, and one year later Wyss observed small hemorrhages and round cell infiltration in the ganglion. In 1874 Jaclard published an account describing hyperemia in the ganglions, intense cellular infiltration of connective tissue, destruction of connective tissue bands and alteration of ganglion cells. Sattler, in 1875, also found infiltration of the ganglion with small round cells, with destruction of ganglion cells and changes in the ophthalmic division of the nerve. Kaposi, in 1876, found hemorrhages in the ganglion, surrounded by areas of exudation and infiltration. Ganglion cells were destroyed, and parts of the ganglion were sclerosed. Chandelux, in 1879, observed similar alterations in the ganglion, as did Leudet, in 1887, and Lesser, in 1881. In 1883 Pitres and Vaillard noted changes in the peripheral nerves, which were confirmed, in 1884, by Curschmann and Eisenlohr. Dubler, in 1884, concluded that the condition was a perineuritis and that the changes in the ganglion were secondary.

Head and Campbell, in 1900, reported detailed observations on the posterior root ganglion, in the posterior root itself, in the peripheral nerves and in the spinal cord in 23 cases and definitely established the pathologic picture. If the patient died at the time of the eruption the ganglion was in a state of severe inflammation. The interstitial tissue was crowded with small round cells, especially at the periphery and in the tissues of the central part of the ganglion, around areas of extravasated blood. The substance of the ganglion might be destroyed to a greater or less extent, but if hemorrhage had occurred at all, it was always present in the dorsal half of the ganglion. In the center of the hemorrhagic focus the ganglion cells were destroyed. In the surrounding zone of small round cells, the remains of ganglion cells were usually evident. The nuclei of the ganglion cells were swollen, the substance of the bodies of these cells were devoid of definite structure, and the chromophilic Nissl particles were not seen. These changes varied in extent in different cases. The sheaths of the inflamed ganglion were invaded with small round cells. The vessels were engorged, and extravasated blood was often seen.

In some cases the inflammation subsided and left no change in the posterior root ganglion. But the greater the severity of the eruption, the more certain were permanent changes to be found in the ganglion. As the inflammation subsided, absorption began. The effused blood underwent retrogressive changes and might remain as a mass of brown granular

material. Ultimately the focus of the inflammation became converted into fibrous tissue, and the extent of this change depended on the severity of the inflammation. If mild, there was little change, if severe, scar tissue formed. In this scar tissue the ganglion cells and nerve fibers were destroyed. The sheath over the scar tissue was thickened and altered in appearance.

Secondary degeneration, similar to changes in the ganglion, occurred in the posterior nerve roots. Head and Campbell showed that the posterior root ganglion was the center of the inflammation, which spread up and down the nerve to some extent. Sometimes the degeneration extended into the posterior column of the cord and down the sensory nerve and its branches to the skin.

Zoster of the branches of the fifth nerve was associated with a similar lesion in the gasserian ganglion, which corresponds to a posterior root ganglion. This lesion caused secondary degeneration in the sensory root of the gasserian ganglion.

The peripheral nerves also showed changes, which could be traced back to the fine twigs that passed into the skin. In time the products of degeneration were removed from the nerve, if the ganglionic lesion was not severe, no abnormality was seen, but if the inflammation was severe, the fibers were replaced with fibrous tissue.

Head and Campbell observed that the changes in the posterior root ganglion resembled closely the changes found in the anterior horn with anterior poliomyelitis. In all their cases the anterior root was normal. Hunt confirmed this observation.

Head and Campbell suggested that the production of the rash was due to an intense irritation in the cells of the ganglion, which normally subserve the function of pain. If the rash were due to increased activity in the posterior root ganglion, causing an increase in the normal trophic impulse, it would be expected to produce a more uniform effect on the skin than it actually did, for the lesions in the ganglion were usually diffuse, and not confined to limited areas.

Head and Campbell concluded that zoster of the branches of the fifth nerve was associated with a lesion in the gasserian ganglion and that the lesion caused secondary degeneration in the sensory root of the gasserian ganglion. They stated the belief that the virus responsible is neurotropic and has a special affinity for spinal ganglions, where changes occur, varying from acute lesions to chronic scar formation.

In cases of symptomatic, or secondary, herpes zoster, Head and Campbell found that the blood supply to the ganglions was definitely disturbed and stated the belief that the process was one of acute destruction of ganglion cells due to vascular changes, rather than of damage by poisoning, with consequent degeneration and death of the cells. The changes in the posterior root ganglion consisted in acute interstitial inflammation, accompanied with necrosis of the ganglion cells. The agent responsible showed a specific attraction for one or more posterior root ganglions, especially those which contained a preponderance of small ganglion cells. They stated the belief that these small cells, among other functions, subserve the pain sense and that their involvement results in the severe neuralgia of zoster. Before the eruption appeared, it was possible to map out the area later occupied by the eruption by means of the hyperalgesia present. They stated the opinion that the eruption was not produced by special trophic nerves but that it was due to the intense irritation of the cells in the ganglion.

Lauber, in 1905, observed necrosis of nerve fibers and evidence of neuritis and perineuritis of the involved branches of the fifth nerve, and in the corresponding portions of the ganglion there were inflammatory and necrotic foci. The neuritic symptoms decreased in proportion to the distance from the ganglion. André-Thomas and Heuyer, in 1912, confirmed the findings of Head and Campbell in a patient who died three days after an eruption of herpes zoster. Similar observations were made by Sunde, in 1913.

Wohlwill reported a fatal case, in which autopsy revealed infiltration of the gasserian ganglion with lymphocytes and plasma cells. The infiltration was confined to a part corresponding to the first branch of the fifth nerve. Infiltration of some intensity was noted in the root of the trigeminal nerve and in the proximal portion of the first branch. The adventitia and media of a small artery in the root showed conspicuous infiltration in the lymphocytes and plasma cells. Fischl found similar conditions in the ganglions and periganglionic tissues, as did Rollet and Colrat, in 1926, and Hesser, in 1924. Kreibitz, in 1938, described a case of a man of 68 who died nine days after an outbreak of bilateral ophthalmic zoster. Practically in their entirety the ganglion cells exhibited granular disintegration of protoplasm and contraction of the nucleus. The pronounced alteration in the peripheral nerves, with extensive demarcating infiltrates, was in contrast to the slight altera-

tions in the gasserian ganglion and indicated clearly that in this instance the initial phenomenon appeared in the skin and the uvea and that the pathologic process then extended centralward

In years past, conflicting theories have been advanced regarding the pathologic process of herpes zoster. Levaditi stated the belief that there was a *tonus immunotrophique* in each spinal segment which prevented infection and that if this was lowered, the organism established itself in the segment of that part of the body supplied by it. Vogt asserted that herpetic diseases were endogenous and that trauma in an area of lowered resistance rendered the area susceptible to viruses already present in the body. Sieu, Poulard and others divided the disease into three forms: a neuritic form, which affects the peripheral branches of the ophthalmic division, a rhizomeric form, which implicates the ganglion, and a metameric form, in which the lesions lie in the pontomedullary nucleus of the fifth nerve.

The point of origin of the disease is not known, whether central, epidermal or neuronal. Most investigators, including Lauber, Wyss, Weidner, Kaposi, and Head and Campbell, have stated the belief that the primary focus was in the ganglion and that the neuritis and degeneration of nerve fibers were secondary developments. They explained the lesions of the skin and cornea solely on a neuritic basis. Some workers believe that a lowered trophic influence permits the entrance of the herpes virus, allowing it to reach the deeper parts in the eye, but this etiologic factor is disputed by most investigators. Pickard did not agree with this assumption because the cutaneous vesicles did not have a uniform effect on the skin. Meller concluded that the epithelial changes were due to trophic disturbances produced by inflammation in the more proximal portion of the nerve. He stated the opinion that inflammatory foci in the ganglion might produce necroses and inflammatory phenomena within the eye without direct extension of the inflammation throughout the course of the nerve. He found characteristic perineuritic infiltration of the ciliary nerves, which could be followed from behind into the interior of the eye, wherever the diseased nerves branched. Gilbert showed sections in a case in which there was perineuritis of the ciliary nerves near the ganglion. Choroiditis was also present, a condition which he felt was primary and the neuritis secondary. He claimed that zoster was a local manifestation of a general disease and that the ocular lesions were probably a perineuritis of the ciliary nerves, a hypothesis

which would account for the deep keratitis and cychitis. Friedreich held a similar opinion. Gardilčić, in 1937, found two areas of necrosis in the sclera which he stated were due to trophic disturbances from diseased nerves. Duke-Elder expressed the belief that ophthalmic zoster was dependent on a trophic disturbance, associated with a radiculoganglionic and sympathetic infection with an unknown virus, and that the essential cause of the neurotropic disturbance was unknown. Van der Scheer, and Aubaret and Margaillan held a similar opinion. According to Sicard, Sicard and Robineau and Vorner, the primary role which the sympathetic nervous system plays in neuralgias due to peripheral neuritis and in vasomotor disturbances which precede the eruption argues in favor of intervention on the radicular sympathetic hilus and serves in part to confirm the theory of ganglioradiculo-sympathetic zoster. With the trigeminal nerves is associated the gasserian ganglion, of the posterior radicular system of the cord. The other, so-called ophthalmic, sphenopalatine and otic, ganglions belong to the sympathetic group and are themselves dependent on the great superior sympathetic cervical ganglion. Accordingly, in ophthalmic zoster there is disharmony between the elements of the sympathetic system and the sensory nerve fibers.

If a neuritic process is present, paralysis of the sphincter of the iris is readily explained. While the ophthalmic nerve contains no motor fibers which supply the intrinsic muscles of the eye, it is known that sensory fibers from the trigeminal nerve reach the ciliary ganglion by way of the ophthalmic nerve. The ciliary ganglion is the actual iridoconstrictor center, which governs movements of contraction of the pupil. A lesion of the ganglion will abolish this contraction, and the tension usually becomes lowered and the pupil dilates under the influence of the dilatory system. Fibers of the trigeminus proceeding from the ophthalmic nerve and extending to the ciliary ganglion are affected by inflammatory lesions, which, in turn, destroy the motor elements of the ganglion.

On the other hand, Dubler, and Curschmann and Eisenlohr maintained that the chief emphasis must be placed on the peripheral neuritis. They asserted that the pathologic process in the ganglion is a probable result of the peripheral changes or may be coordinate with them. Wilbrand and Saenger accepted this view but were not quite so positive about the neuritis. Orr and Rows, and Montgomery and Culver also stated that the disturbance was an ascending process.

Teague and Goodpasture stated the opinion that the virus incubated at the site of the inoculation passed along the afferent nerve to the ciliary ganglion, producing hemorrhagic inflammation, and then proceeded along branches of that ganglion to the skin, where the vesicles developed. Marianesco and Draganesco stated that the infection was located in the sensitive nerve endings and secondarily involved the motor nerves, with dissemination by the veins and lymphatics. They traced the infection along ciliary nerves to the meninges. Sedan was of the opinion that the virus was transmitted to the ciliary ganglion over sensory nerve fibers from the nasociliary nerve of the fifth nerve.

Wohlwill expressed the belief that the disease was due to an ascending infection, utilizing the lymphatics of the nerves. He stated that disease of the primary sensory neuron was necessary for the development of zoster but that it alone was not capable of producing the cutaneous picture, in his opinion, it prepared the soil for the virus, which produced the vesicles. This preparation of the soil apparently occurred through reflex disturbance of vasomotor innervation. Wohlwill assumed a reflex causation of the cutaneous lesions by vasomotor disturbance and stated that this phase might come to an end as soon as the reflex arc was interrupted, by the complete degeneration of some of the sensory components. Montgomery claimed that the zoster virus had a special affinity for nerve tissue.

Some investigators believe the disease to be due to irritation of vasodilator fibers, and not to an extension of inflammation to the terminal filaments of nerves in the skin, and they are of the opinion that the eruption is caused by inflammation of the sympathetic fibers distributed through the arteries which produces distention and possible rupture of the capillaries. The sympathetic fibers arise from the superior cervical ganglion and pass along the nerve to the terminal branches of the ophthalmic artery. As the inflammatory process affects the ganglion and nerve, the accompanying sympathetic, vasodilator, fibers are affected, leading to vasodilation. They hold that the pathologic process is induced by excess fullness of certain vascular regions and is characterized by areas of vesicles and subepithelial infiltration. The exponents of this vasomotor theory are von Recklinghausen, Ebstein and Abadie, von Tschermak, Wohlwill, Aubineau, Nobl and others.

In 1898, Abadie expressed the opinion that herpes zoster ophthalmicus was provoked by a pathologic state of the arteries and that lesions of the ophthalmic artery and its branches were

the cause of the zoster phenomena. He stated the belief that the eruption was due to vasomotor disturbances and attributed the limitation of the eruption in the area of distribution of the ophthalmic nerve to disturbance of the sympathetic fibers accompanying the arteries in this region. He pointed out that the vessels in the area innervated by the maxillary branches of the fifth nerve receive their vasomotor nerves from a different sympathetic source. But this would not explain the corneal lesions or the corneal anesthesia. He stated that the ganglion was altered by obliteration of its nutrient vessels. He expressed the belief that the ocular paralyses were also secondary to vascular lesions and were not due to extension of the infection from sensory nerves to motor nerves in the orbit or the cranium. Aubineau agreed with this theory and reported autopsy observations in detail. He noted that the arteries of the brain were atheromatous and dilated, with numerous leukocytes in their lumens and with periarteritis, revealed by an abundance of cellular elements and by hemorrhages at the periphery of the vessels. A thrombus was noted in the extremity of the ophthalmic artery, with thickening of the intima, and similar changes were observed in the smaller ramifications. The gasserian and ophthalmic ganglions showed vascular lesions of endarteritis and periarteritis. The nerve sheaths were thickened and infiltrated with cells in the process of multiplication. There were zones in the ganglions in which round cells presented clearly the aspect of lymphocytes. The arterioles near the ganglions exhibited proliferated endothelium, and some sections revealed minute hemorrhagic foci between the cells. An irritative or infectious process extended to the vessels and nerves of the muscles and to connective tissue which separated muscle fasciae. In the muscles were noted masses of lymphocytes, indicative of inflammatory foci, while muscle fasciae, instead of lying side by side, were frequently separated by new-formed connective tissue. The arteries and arterioles were all altered, and nerve bundles exhibited thickening and cellular multiplication of their sheaths. These examinations demonstrated a constant predominance of arterial lesions. Nobl, in 1911, argued that herpes zoster is a vasomotor disturbance, he stated that if zoster is regarded as a vasomotor phenomenon, it is possible that at one time various nerve centers of unequal sensitiveness are stimulated and injured, in varying degrees. His explanation is that the initial inflammatory, angioneurotic injury to the vessel wall is to be considered as an expression of a sympathetic reflex neurosis, which leads first



to edema from vascular dilatation, and later to the epithelial neurosis. The irritation of the sympathetic vasodilator center is distributed through the avenues of sensation, whereby the disease of the spinal ganglions occasions the afferent irritation of the reflexes. Then the excitant acts with increasing intensity on the spinal cord and extends to the sympathetic ganglions. It is by irritation of the latter that the vasomotor phenomenon occurs. The return of the phenomenon to the source of the irritation explains the intense local appearance of the eruption in the skin of the corresponding nerve.

Kreibich observed that in the terminal stages of dementia paralytica there is often associated a typical herpes zoster, which he stated to be due to vasomotor changes in the skin associated with organic nervous disease. He concluded that vasomotor changes are a reflex phenomenon, set off by irritation of any part of the afferent limb of the reflex arc. He stated the belief that centrally arising stimuli were capable of setting off vasomotor reflexes. Arnstein agreed with Kreibich that the cutaneous lesions occur through irritation of the Kreibich reflex arc at any point of its afferent, efferent or central connection. Zee-man stated that the anoxemia of the involved tissue, produced by vasomotor spasm, is responsible for the epithelial changes, in conjunction with toxins liberated by the etiologic agent within the nerve. Bézi expressed the belief that occlusion of a vessel produced hemorrhagic necrosis, with a leukocytic zone, and that purulent inflammation followed. He concluded that the central process antedated the peripheral pain and the cutaneous eruption.

Kundratitz, however, claimed to be able to demonstrate that the virus is in the vesicle, if this is so, the cutaneous lesions are not trophic or vasoparalytic, as many believe.

It has proved impossible for most investigators to reproduce the disease experimentally, or at least to obtain transmission in series. Accordingly, the nature of the zoster virus is unknown, but the disease is assumed to be a specific infectious process, due to a nonfiltrable neurotropic virus.

However, Rosenow and Oftedal made a complete report on their experimental work, in which they endeavored to prove that herpes zoster was a streptococic infection, gaining entrance to the circulation through diseased tonsils or pockets of pyorrhea and possessing an elective affinity for the posterior root ganglions. In animals, they produced typical herpetic lesions centrally and peripherally by intraperitoneal and subcutaneous injections. The ganglions corresponding to the

herpetic area in the skin showed hemorrhage and edema. Guiter claimed to have produced an eruption of herpes zoster by injection of a suspension of brain substance from animals which were infected with herpes zoster. Flexner, and Teague, Goodpasture and Lipschutz reported that they produced the disease in animals by inoculation of the virus. Goodpasture claimed to have demonstrated the presence of the virus in the intervertebral ganglions, as well as in the vesicles. Kuchner, in 1933, stated that he had produced the disease in the corneas of rabbits by applying scrapings of epithelium from the corneas of 36 patients with herpes zoster. Von Szily reported having produced uveitis in the eyes of rabbits with virus from patients with herpes zoster, which uveitis was transmitted to the opposite eye, giving a clinical and histologic picture resembling that of sympathetic ophthalmia. This claim was confirmed later by experiments by Gifford and Lucic, in 1927, showing that the extension occurred via the optic nerve and the optic chiasm to the other eye.

Sunde, in 1913, reported observations at autopsy, made three days after the infection. The gasserian ganglion was twice the size of that on the other side. Sections showed hemorrhagic points, and microscopic examination revealed acute inflammation, hyperemia, round cell infiltration, capillary hemorrhage and fibropurulent exudate. In all sections gram-positive cocci were found, some in short chains. Bézi reported similar findings seventeen days after the initial infection. In the medial two thirds of the ganglion was observed a fibrinopurulent exudate with pronounced hemorrhage. In the sheath of the third nerve a similar purulent exudate was noted. Many large cells containing fat granules surrounded the degenerated myelin sheaths. Bézi demonstrated many bacteria in the areas of degenerated myelin sheaths, predominantly lancet-shaped, gram-positive diplococci. On the other hand, Magnus, in 1902, 1903 and 1906, found no organisms in the ganglions of the posterior horns, and Scheel, in 1904, and Arent de Besche, in 1910, were also unsuccessful in their search. Freund, in 1928, reported 2 cases and found no proof that the etiologic agent was demonstrable in the fluid of the zoster vesicle.

#### CUTANEOUS LESIONS

Head showed that an unruptured cutaneous vesicle was divided by small septums, extending from the roof to the floor and that in the floor were masses of round cells. The external covering of the vesicle consisted of the non-nucleated cells which made up the epidermis. Head stated



the belief that the septums were due to partially raised epithelial cells which retained their attachment to the roof and the floor. The vesicle was a cavity with incomplete partitions, formed by altered epithelial cells attached to the roof. It contained epithelial cells of all ages, which showed a nucleus, and many leukocytes derived from the vessels. The papillae below the vesicles were engorged with blood and contained many leukocytes.

When a vesicle is changing to a pustule, the cells in the septums increase and push apart the epithelial cells on the floor of the vesicle. The cells are often so enlarged as to contain several nuclei and surround the nerve trunks and press on the nerve covering. This causes the fine nerve twigs in the deeper layers of the corium to show swelling of the neurilemma, with degenerated myelin sheath, and results in disappearance of the white substance of Schwann, leaving the axis-cylinder swollen and bare. The larger branches also show conspicuous degenerative changes. Oliver stated that these changes produce the severe attacks of neuralgia which precede or accompany the eruption.

The changes in the skin are usually found in the rete layer of the epidermis. The epithelial cells assume various shapes as a result of traction; these are degenerated cells. In these cells, in and around the vesicles, are found inclusion bodies, resembling protozoa, at first thought to represent parasitic cell inclusions but now considered merely as degenerative changes. Sections of the skin through lesions show that the vessels are dilated and surrounded by lymphocytes and leukocytes. The vessel walls are edematous, and the internal cells of the walls are swollen.

#### OPTIC NERVE, RETINA AND CHOROID

In some cases the optic nerve has been involved during the process, and this may be due to the fact that the organism may spread locally from the posterior, or gasserian, ganglion to adjoining structures. The optic nerve and the gasserian ganglion are very close together, and this may account for the presence of blindness in some cases, the result either of the toxin or of the specific virus involving nearby structures. Wyss, in 1871, reported that the choroid showed extravasation of blood and leukocytes. Meller, in 1920, found small foci of round cells around the vessels in the choroid, which were confined almost entirely to the middle and outer layers. The outer layers of the retina were normal, the stratum fibers of optic nerve were atrophic, and in some places perivascular infiltration was apparent. Head and Campbell did not find the retina and choroid involved in any of their cases, but in 1

case the optic papilla showed edema and contained a few round cells. The optic nerve showed destruction of fibrils of the medullary sheaths of the nerve fibers. In some cases the ciliary nerves were surrounded by a sheath of mononuclear cells. Gilbert observed that horizontal sections through the eye at the level of the optic nerve showed pronounced perineural infiltrations. The sections, which included ciliary nerves in their oblique course through the sclera or between the sclera and the choroid, showed some marked inflammatory changes in and around the nerves. The nerves during their oblique course in the sclera were cuffed with round cells. When one of the nerves lay close to the choroid, the inflammation involved the choroid, more specifically the suprachoroid and the layer of large vessels, where the infiltration became primarily intervascular, rather than perivascular. Accumulations of round cells occurred in sections of the ciliary nerves in the upper half of the bulb, posterior to the ciliary processes. Gardilčić, in 1937, noted similar changes. Kreibitz, in 1938, found that the posterior ciliary nerves presented, in part, similar conspicuous alterations, necrosis and areas of infiltration. These investigators observed perineuritis infiltrates and infiltrates in the nerve itself, with small hemorrhages. Small nerve bundles, likewise densely infiltrated, were traceable from the region of entrance of the optic nerve to the ciliary body. Numerous perivascular infiltrates, unassociated with nerve fibers, were also observed. Meller was able to follow the perineuritic infiltrations into the interior of the eye, an observation which would explain the many infiltrations of the sclera, choroid, cornea and iris, with resulting necrosis.

#### IRIS AND CILIARY BODY

Wyss, in 1871, reported that the iris showed numerous lymphocytes on its anterior surface. Head and Campbell found that the iris was necrosed, as well as nearby portions of the ciliary body and the sclera. Meller, in 1920, observed that the iris was necrotic, with irregular scattering of pigment, and that the ciliary body showed many foci of round cells in atrophic muscle fibers. The vessel walls showed hyaline degeneration and were thickened. Kreibitz found that the iris exhibited near the root two small areas of necrosis. The ciliary body was found, to a large extent, to be necrotic and to be surrounded by a dense wall of infiltrate.

#### GLAUCOMA

Disturbances of ocular tension in cases of herpes zoster have for several years been the ob-

ject of investigations, the results of which have added to knowledge of the physiopathology of the sympathetic nervous system. The pathologic nature of the glaucomatous complications is obscure, although several hypotheses have been considered. Some workers believe that the inflammatory process from the gasserian ganglion extends along the nerves to the globe of the eye itself. Others believe that the acute form of glaucoma is the result of a disturbance of the sympathetic nervous system. While the action of the sympathetic nervous system in the control of ocular tension is not as yet clearly understood, the glaucoma which supervenes in cases of ophthalmic zoster ordinarily is related to sympathetic excitation. However, it appears that regulation of ocular tension is not controlled by the sympathetic system exclusively, and it is possible that the zoster virus may act on tension of the eye by way of other nerve filaments. Experimental retro-gasserian neurotomy is accompanied with diminution of ocular tension. Excitation of the root of the trigeminus immediately beyond the protuberance raises ocular tension, while its section lowers the tension. As a result, zoster should be accompanied, rather, with diminution of tension.

#### CORNEA

Biozzi expressed the opinion that trophic disturbances in the cornea arise through a nerve filament which connects the sphenopalatine with the ciliary ganglion, but this filament is not constant, a fact which explains why the cornea does not in all cases participate in the sphenopalatine syndrome. Head and Campbell stated that the corneal lesion was a subepithelial infiltration in the substantia propria, occurring around the terminal nerve fibers, which resulted in vesicles and secondary infection, or it might lead to keratitis profunda, iridocyclitis, increase in tension, optic nerve atrophy and motor paralysis. Reiser showed that after destruction of the gasserian ganglion the first sign of degeneration of corneal nerves appeared in twenty-four hours. After sixty hours hardly a single fiber of the thick corneal nerve bundles was intact. The signs of degeneration lessened toward the periphery of the nerve elements, while the terminal nerve fibers showed no signs whatever of degeneration. This power of resistance is due to the syncytial structures and has been known for some time. The few fibers which enter the cornea from the conjunctiva suffice to provide the nerve supply to the corneal cells by way of the terminal reticulum, which remains intact after section of the afferent nerves.

One is accustomed to think of sensory nerves as conveying only afferent impulses. Broadbent, in 1866, stated that in cases of herpes zoster the sensory nerves may conduct influences or impressions from, as well as toward, the nerve centers. Parsons expressed the belief that the transmission of impulses also may proceed in the opposite direction. Bayliss called these efferent impulses in afferent nerves antidromic impulses. He suggested the term "antidromic" for the process by which nerve fibers convey impulses in a direction opposite that assumed by the Bell-Majendie law when such impulses produce effects in the organs of origin of such fibers, that is, when afferent fibers excited at their ends, in the central nervous system, produce vascular dilation at their peripheral ends, in the body tissues. These posterior root fibers are no doubt capable of carrying impulses in both directions—afferent sensory impulses from the periphery to the central nervous system, and efferent vasodilator impulses from the central nervous system to the periphery.

Bruce carried out a series of experiments to show that these sensory fibers must bifurcate at their extremities at the periphery of the body, one branch ending in the sensory end organs in the skin and the other ending in the vessels. The former carries sensory impulses centralward, and the latter carries vasodilator impulses to the periphery. The common stem carries impulses in an ascending and a descending direction. If the cells of the posterior root ganglion are irritated, they will be capable of originating impulses which pass in two directions, one centralward, causing the pain, and the other peripherally, along fibers to the bifurcation, from which a twig passes to a vessel and produces dilation. Severe involvement of the ganglion gives rise to extensive eruption, and smaller lesions are associated with smaller eruptions. Teague, Goodpasture and Lipschutz stated the belief that the virus followed the nerve and penetrated the intervertebral ganglion and that it must have traversed the same route in an opposite direction in order to produce herpes zoster in the corresponding cutaneous region. This assumption they proved experimentally. Groups of vesicular elements, confined to one side of the trunk, made their appearance in guinea pigs and rabbits in consequence of the introduction of virus at one point of the corresponding region. In forty-eight hours groups of vesicles formed at a distance in the ventral and in the dorsal region but never extended beyond the median line. These lesions exhibited all the characteristics and distribution of herpes zoster.

## ADJACENT GANGLIONS

Although the specific inflammation attacks chiefly one sensory ganglion, the adjacent ganglions may not always escape involvement. This explains those cases in which the eruption is in the zone of one ganglion and complications occur which can be attributed to involvement of other ganglions. Multiple involvement of these ganglions is not infrequent, thus producing a variety of clinical combinations. From considerations of cases, the symptoms of herpes zoster ophthalmicus of the face, neck, ear, mouth, eye and nose may occur together in almost every possible combination.

## SPINAL FLUID AND BLOOD

In cases of herpes zoster ophthalmicus the cerebrospinal fluid is modified, and this is not surprising, after inflammatory changes and degeneration in the posterior roots and posterior columns of the cord have taken place. The cul-de-sacs of the pia-arachnoid bathe the gasserian ganglion, and the inflammatory ganglionic process may, according to its intensity, provoke reaction in the spinal fluid, causing lymphocytosis and albuminosis. Brown and Dujardin reported on a study of the cellular elements in the spinal fluid in 42 cases, with inconstant results. In the majority of cases a lymphocytosis occurred, which showed no relation to the intensity of the eruption. In the majority of cases there was a slight increase in the albumin, and in 1 case there was an increase in the globulin content. Similar studies by numerous investigators—Corson and Knowles, Hunt, Achard, Jacquet and Bariety, Touraine and Baumgartner, Chauffard and Rendu and others—have been described in the literature. Aubaret and Mastier found an increase of tension in the spinal fluid with the manometer of Claude, as did Rollet and Colrat. Some authors have described a reduction of tension.

Glaubersohn and Rabinowicz found, in most cases, a slight decrease in neutrophils and a pronounced increase in lymphocytes. They noted leukocytosis from the first to the fifth day, with the peak on the third day. From the fifth to the eighth day, there was a normal white cell count or leukopenia, with polymorphonuclear leukocytes predominating and decrease of eosinophils, was present. On the eighth to the twelfth day during the stage of drying of the vesicles a leukocytosis, often with an increase of eosinophils, was noted. Keining and Steiger-Kazal made similar observations.

## PROGNOSIS

In consideration of ocular complications which may develop during the eruption or afterward, the prognosis with respect to vision is reserved. It requires careful observation of the patient long after the disappearance of the zoster for the purpose of detection of the disturbances of corneal sensitivity. The prognosis in cases of corneal ulceration may be serious, as corneal opacity may result, in whole or in part, and may become permanent, with serious loss of vision unless requisite precautions have been instituted. When the eye becomes inflamed with the appearance of the cutaneous eruption the cornea is usually severely affected and gives rise to various ocular pictures, but, as a rule, when the cornea does not become inflamed until the termination of the attack, the symptoms are less severe. Corneal ulcerations may become secondarily infected, terminating in iridocyclitis, glaucoma or perforation. Certain lesions may appear in the absence of any superficial lesions, such as primary iritis, keratitis or glaucoma. While ocular lesions are most frequently benign, they may suddenly become grave. The prognosis is grave when iritis develops, for the eye may continue to be irritable and subject to high tension, with glaucoma developing. The attack may last from a few weeks to several months. Severe neuralgic pains with anesthesia may persist, and the exhaustion subsequent on continual pain may be a serious factor. Violent delirium has been known to occur, and suicide has been reported in some cases.

Aside from the serious risks which optic neuritis may offer for function of the eye, it involves an unfavorable prognosis for the future. Only rarely does visual function recover even a traction of its normal integrity. When loss of the eye is not complete, vision is always impaired.

A reserved prognosis is necessary when ophthalmoplegic symptoms which do not recede completely are observed during the course of the eruption. All paralytic phenomena constitute a highly important element in prognosis from the viewpoint of a nervous disturbance, which may arise in a more or less remote future. Muscular complications may be divided into two categories: those which tend toward complete recovery, and those which are followed by more or less permanent disturbances, after some improvement. In some cases a certain degree of paresis may become permanent. This entails a hazard to future motility and may occasion subsequently even graver disturbances, which may prove fatal.

## DIAGNOSIS

The diagnosis of herpes zoster ophthalmicus is based on symptoms and on the evolution of the disease. Sometimes the sequelae render possible a late diagnosis. As a rule, there is no confusion in the diagnosis provided that a thorough examination of the functional state of the eye is conducted in every instance of a zoster eruption. A careful test of visual acuity should be instituted first, and afterward tests for binocular vision and motility should be performed, whereupon the existence of a slight degree of diplopia or of a strabismic deviation will be readily recognized.

Herpes zoster ophthalmicus has been mistaken for erysipelas, supraorbital neuralgia, disease of the frontal sinus, migraine headache, eczema, cyclitis, dacryocystitis, impetigo, sinus thrombosis, cerebral tumor, meningitis and herpes simplex. In erysipelas, there are large bullae, and the skin is greatly swollen. The eruption is not limited to the midline, it affects both sides and assumes the aspect of the wings of a butterfly. The fever is higher, and the pain is absent. The condition may be confused with herpes simplex on account of the localization of the latter and the nervous disturbances associated with it. Herpes simplex is, however, not accompanied with neuralgic pains. Impetigo exhibits its characteristic crusts and may be localized in any part of the face. In some cases, in which an associated unilateral paralysis of the ocular muscles exists, aseptic thrombosis in the cavernous sinus must be considered. In a case of this type, there are marked chemosis, and frequently exophthalmos, and the symptoms are often bilateral. Thrombosis of the lateral sinus can usually be eliminated by roentgenograms. Slow hemorrhage from an aneurysm of the internal carotid artery or from the circle of Willis gives a similar picture. Cerebral tumor can usually be eliminated by the history of sudden onset, negative roentgenograms and absence of signs of intracranial pressure. The fifth nerve sends a branch to the meninges, and often severe local meningitis may accompany the disease.

## TREATMENT

In an attempt to determine what course of treatment should be followed in the future in cases of ophthalmic zoster, the results and types of therapy employed in past years have been analyzed. A specific treatment for herpes zoster is not available, and one must choose from a wide variety of therapeutic measures. A vast number of remedies have been suggested for this disease, but no one of them has been successful in all cases. The treatment of zoster has been largely

symptomatic and has been directed chiefly to the relief of pain. The general treatment consists of rest in bed, light diet, sedatives and supportive measures. Salicylates, quinine, bromide, iodides, barbiturates and arsenic have been used as alteratives, with beneficial effect.

Early protection of the cornea prevents its superficial involvement in many cases. The cornea can often be protected by the use of ointments, and atropine is often indicated. If ulcers develop and are deep, suturing of the lids may be necessary. Rea advised bandaging the eye from the start, for a period of several weeks or months. He recommended daily irrigations with a mild solution of boric acid and use of a mild ointment between the lids.

If hypertonia is present, miotics are indicated in some cases. The use of warm compresses is often advisable. Mild proteïn silver U S P, neo-silvol, ethylmorphine hydrochloride, phenacaine hydrochloride and ethylhydrocupreine hydrochloride have all been used, with benefit in some cases. Pierron advised touching up the ulcers of the cornea with 1:1,000 solution of methylthionine hydrochloride or tincture of iodine and applying ointment of ichthammol, 1:200, between the lids. Ammoniated mercury ointment and ointment of scarlet red have also been recommended by some authors. Burwell, in 1922, advised the use of subconjunctival injections of isotonic solution of sodium chloride and an occasional injection of 1 per cent guaiacol and ethylmorphine hydrochloride if corneal lesions were present.

Many types of treatment have been advised for the cutaneous lesions. Some authors prefer various powders, others use oils to prevent drying of the secretions. Painting of the vesicles with collodion has been advised, but it may increase the pain temporarily by contracting the skin in the vicinity. Fox, in 1922, advised a mixture containing liquid petrolatum. Others have recommended the use of 5 per cent silver nitrate, a weak solution of iodine, a weak solution of phenol, tincture of benzoin, hydrogen peroxide or sterile olive oil. Employment of pure alcohol was advised by Reynolds. Bayer painted the vesicles with ointment of ichthammol. Cocaine and zinc oxide ointment have been used occasionally, with success. Astringent powders have been advised by Morax, Fuchs and Rollet. Oils and petroleum were advised by Doggart, Darier and de Schweinitz. Some physicians apply zinc stearate, starch and talc over the surface of the skin each day, and others prefer bismuth tribromphenate. Calamine lotion, 2 per cent gentian violet medicinal, diluted solution of lead

subacetate and tincture of opium U S P , potassium permanganate, 1 4,000, and various other lotions and powders have been tried

In 1938 Hollander introduced the treatment of anesthetization of hyperesthetic areas of the skin for the relief of pain. These areas are located about the papules and vesicles of the herpetic rash. In all his cases the pain did not return, either during or after the resolution of the lesions. When every hyperesthetic zone is anesthetized, the pain is completely relieved. He employed 5 per cent benzyl alcohol, 3 per cent ethyl amino-benzoate and 1 per cent phenol in expressed oil of almond. He injected 0.5 cc of the preparation per square inch of surface, just under the corium. Secunda, Wolf and Price treated several patients with a subcutaneous injection of 1 to 2 per cent solution of procaine hydrochloride under the inflammatory tissue, with complete relief of pain, and in most cases the relief was permanent. The clinical course of the cutaneous lesions was not affected. Rosenak reported relief of pain and regression of vesicles after intervertebral and paravertebral injections of a 0.5 per cent aqueous solution of procaine hydrochloride. Pillsbury and Fonde advised the use of an ointment containing 1 per cent nupercaine hydrochloride in small amounts, rubbed into the skin.

The beneficial effects of thiamine hydrochloride in cases of neuritis and its value in prevention of certain degenerative changes are acknowledged, and as the prominent feature of herpes zoster is neuritis and a degenerative change, many investigators have used it, with good results. Pain is often definitely relieved. Nitzulescu and Triandaf, Carlevaro, Vorhaus and Viallefont reported good results with thiamine hydrochloride, aminothionine and thiosinamine. Thiamine hydrochloride, 5 to 10 mg, is often injected subcutaneously daily for six days. Goodman treated 5 patients with thiamine hydrochloride, with excellent results. He used six or seven subcutaneous injections of 3,000 units. The injections were administered daily. He claimed that the pain was relieved promptly and the lesions of the skin cleared up earlier. Ascorbic acid has been used by some investigators. Dainow, in 1936, claimed to obtain a more rapid evolution of the disease through repeated intravenous injections of from 10 to 15 cc of the substance. Some patients received as high as twenty-five injections. Its influence is assumed to be due to the fact that vitamin C acts directly on the hypothetic virus of zoster.

Vendel, in 1923, was one of the first to enumerate the benefits of solution of posterior pituitary U S P (surgical) for herpes zoster. He

advised daily injections of 0.5 to 1 cc. Sidlick advised two injections of the substance, a day apart. Numerous investigators have reported good results with this treatment, among them, Somers and Pouppirt, Gifford, and Niles. The action of solution of posterior pituitary is directed against the symptom of pain, but it has no effect on the course of the disease. This treatment is contraindicated in cases of hypertension, increased intracranial pressure or pregnancy.

Rollet, LaChaise, Pierron, Badeaux and Stumpf reported good results with radiotherapy for the relief of the neuralgia. Lane recommended radium and reported its use in 5 cases of herpes zoster, with good results.

Heavy doses of roentgen rays are used to relieve pain and reduce the intraocular tension in cases of herpes zoster. High voltage roentgen therapy has been advised by Schamberg, Secunda, Wolf and Price, Darier, Milian, Meller, Keichline, Lloyd, Pardee, Pendergrass, and others. Stephenson, in 1928, noted the early relief of pain with roentgen rays, and he claimed that it shortened the course of the disease. Foveau de Courmelles also reported excellent results with this treatment in the relief of pain following ophthalmic zoster. He expressed the belief that the doses applied should differ according to the individual patient and that a tentative dosage is required for each patient. He stated that investigation of the conditions of the skin, digestive apparatus and cutaneous reactions is necessary. With these data, the operator is able to determine whether to apply soft rays or hard, penetrating rays. Filtration is essential and should be adapted to each patient. He claimed to have had successful results in 80 per cent of cases of herpes zoster, relieving pain and neuralgia in a short time, as well as hastening recovery. Badeaux, in 1935, reported excellent results with roentgen therapy in 4 cases of ophthalmic zoster. The pain ceased in twenty-four hours, and in four or five days the cutaneous lesions were dry and the corneal ulcers had healed. The factors used were as follows: 110 kilovolt peaks, 5 milliamperes intensity, 4 or 5 mm aluminum filter, exposure time of four to six minutes, varying with the region or the case, and anode-skin distance of 10 inches (25.4 cm). Roentgen irradiation for postzoster neuritis and irradiation of the ganglions have reduced the intensity of the disease and relieved pain. Vignal was one of the first to use roentgen radiation for the relief of pain of herpes zoster, and he expressed the belief that its value lay in the specific effect on resorption of a round cell infiltrate in the spinal ganglions and the posterior spinal nerve roots.



High frequency currents have proved serviceable. Buckley, in 1874, was the first to use galvanic current in cases of this disease for relief of pain. W. O. Moore later reported good results, as did Sutton, using 5 milliamperes in the treatment. Tsiexhanovich, in 1897, and Menacho, in 1902, claimed good results with electrotherapy. Letulle, in 1882, reported successful use of the faradic current. Violet radiation has been advocated by some because it is rapid in action and effective against pain and its use avoids indelible scars.

Gruter used short wave rays from twenty to twenty-five minutes, with success, in a case of herpes zoster. These rays produced edema of the cornea and iris, but the herpetic infiltration in the parenchyma cleared rapidly. No burns of ocular tissue were observed. He concluded that the biologic action of the rays was due to the intense warmth penetrating into the depth of the tissues, by which the growth of bacteria was stopped, and to the intense increase in the circulation of lymph. The latter was manifested in a rather protracted edema in the corneal tissues.

Falcão, in 1927, reported excellent results with rays of a Hanau lamp, at a distance of 60 cm. The pain disappeared after two treatments, and after seven applications the eruption had healed, without trace of any scars. Lloyd advised the use of radiant heat, an infra-red lamp or Thermolite. Jacobson, in 1926, obtained good results with the daily use of a 1,000 watt red globe for twenty minutes. A few such applications healed the lesions and removed the pain. L. Coppez advised diathermy for herpes zoster ophthalmicus. This consisted in the employment of currents of low tension and high frequency. This treatment was used in 4 cases, with gratifying results. Ebert, in 1941, also reported good results with diathermy for the relief of pain. MacNab and Ettles used ionic medication in several cases, with benefit. The neuralgic pain and disturbed sensibility disappeared almost at once.

Marlow observed 4 cases in which treatment consisted of intramuscular injections of arsphenamine (0.6 Gm.) and mentioned 5 other cases reported by Milhan in which this therapy was used, with striking results. In twenty-four hours the pain was much diminished, and in twenty-four hours more it was completely relieved. In each case the eruption of the skin cleared within a few days. All showed large areas of epithelial disturbance of the cornea, which healed with an insignificant scar and with little visual loss. Gebb, as did Yanes, reported good results with neoarsphenamine, which brought about immediate improvement in the cutaneous lesions but had no effect on the ulcerations. Agnello claimed similar

results. Romer and Zangger each recommended arsenical preparations for internal use during the course of the disease. Elliot claimed that solution of arsenic and mercuric iodides U. S. P., 10 minims (0.62 cc.), three times daily in water after meals, was a specific for pain in this disease and helped very much the clinical course. Torres, in 1936, reported good results with injection of 3 cc. of Arsaminol (arsphenamine), which gave marked relief in twenty-four hours. He concluded this preparation of arsphenamine represented an extraordinarily efficacious therapeutic agent for this disease. Mildenerger, in 1937, used intravenous doses of Atophanyl (product containing cinchophen sodium, sodium salicylate and paraaminobenzoyl diethyl aminoethanol), with excellent results. Endoarsen (a product containing a cacodylate combined with mercury and iodide) also has been recommended. Fournier reported good results with intravenous injections of iodobenzomethylformine. The pain disappeared in twenty-four hours. Treatments were given daily for four days, and by this time the lesions of the skin had largely faded.

Bénard and Joltrain, in 1927, reported good results with the use of intravenous injections of the sulfurous and isotonic water from springs at Uriage, France, 10 cc. doses were given.

Richman, Beam and Lindberg, and Walker and Walker reported successful treatment with injections of 5,000 units of diphtheria antitoxin given intramuscularly. Two such treatments were given, as a rule, during forty-eight hours. They claimed that the subjective and objective symptoms abated almost at once. Berrisford, in 1935, reported 4 cases, in which he gave three intravenous injections of triple typhoid vaccine during the course of seven days. He described glowing results with this treatment.

Phillips and Morginson, in 1932, advocated the use of sodium iodide. The drug was used intravenously in 2 Gm. or 31 grain doses on alternate days, for from five to seven injections, or until relief was obtained. Pain usually disappeared after the first treatment. Lockwood, Ruggles and Powell reported good results with this type of treatment. Sindhu used the same treatment combined with 1 cc. of solution of posterior pituitary U. S. P. given subcutaneously, the treatment being repeated in two days. Stastnik treated 5 patients, in 1935, with a 20 per cent solution of sodium thiosulfate administered intravenously. Four to twenty injections were given, daily or every other day, depending on the severity of the ocular infection. Other authors used quinine, salicylates, theosinamine, ethyl chloride and iodine preparations. Junius



reported good results with lactic acid, which he claimed were due to its altering effect. Renard advised against the use of local treatment if there was any motor disturbance of the pupil or oculomotor paralysis, but urged mercurial therapy.

Grandi, in 1937, used intramuscular injections of Protinal for pain. J. Rollet and Parthiot, and Sarkovski recommended injections of procaine along the course of the nerve, while Rasquin, Michelsen, Vincent, W. Harris and Frazier advised injection of alcohol into the nerve. Johansson, in 1936, used Impletol (a combination of procaine hydrochloride and caffeine) to relieve pain, with satisfactory results. Duke, in 1924, advised use of epinephrine subcutaneously, 0.5 cc every five minutes until the patient was relieved or until a tremor appeared. This had no effect on the cutaneous lesions. If the drug was given in adequate doses, Duke claimed that the relief of pain was prompt in 50 per cent of cases.

Francois, in 1936, used subcutaneous injections of antistaphylococcus vaccine in the vicinity of the eruption, with good results. Fouassier, in the same year, saw a case in a female who was successfully treated by intradermal injection of this vaccine. In order to prevent local and general reactions and to avoid the painful subcutaneous injections, he used 1 drop of the vaccine intradermally, in the vicinity of the largest pustule, the injection being repeated every two days and increased each time by 1 drop. Improvement was noted on the third day. The pains had disappeared and the swelling lessened. At the time of the sixth injection, of 6 drops, the patient appeared cured. Four supplementary injections of 6 drops were given on alternate days. The author expressed the belief that the superiority of this treatment provided protection for the organism against infection, simultaneously with promotion of rapid and complete disappearance of pain. Godal and Magiou, in 1937, used the same treatment, with good results. From their experience with vaccino-therapy of zoster, they were of the opinion that the evolution of the disease was curtailed thereby, at least so far as acute symptoms were concerned. The pain was alleviated almost immediately, and the lesions dried up more rapidly than normally. The relief of pain preceded that of the dermatitis. They stated the opinion that the amount of vaccine should vary according to the intensity of the zoster. They thought that the action of the vaccine served to abort the zoster promptly, thus preventing the more or less grave ocular complications, which are always to be apprehended. They began treatment with 0.5 cc of antistaphylococcus vaccine injected into the

forearm. On the following day they gave 0.75 cc, and then 1 cc for the next four days.

In patients who suffer from persistent pains, accompanied with keratitis, it is often necessary to protect the cornea by a median tarsorrhaphy, not only during the course of zoster but even for many years afterward. Long external blepharorrhaphy is successful in many cases. Cross, in 1918, performed pericorneal neurotomy in a patient for relief of constant pain and corneal ulcer. Relief of pain was immediate, and the ulcer healed in seventy-two hours. Lodge and Lodge sutured the lids to relieve pain, and corneal ulcers were checked and repair followed rapidly. Badot recommended removal of the central portion of the ophthalmic branch of the trigeminal nerve in cases of severe zoster. Peet, in 1929, sectioned the sensory root of the gasserian ganglion in 2 cases of postherpetic trigeminal neuralgia.

Bryan, in 1923, reported a case of zoster in a male involving the first and second branches of the nerve. Pain in the eye was relieved by cocaineization of the nasal ganglion, and to relieve the pain in the distribution of the supraorbital and frontal nerves, the ophthalmic division of the fifth nerve was reached with cocaine through the sphenoid ostium. This gave instant relief, and some time later the same procedure was repeated with success. When the procedure was repeated the second time, the ophthalmic division was cocaineized as before, but this did not relieve the pain in the eye until the nasal ganglion was cocaineized. The nasal ganglion is the sympathetic ganglion of the maxillary division, corresponding to the ciliary ganglion of the ophthalmic division. Sicard and Robineau, in 1922, reported 3 cases in which persistent neuralgic pain continued for years after the disease had subsided. Gasserectomy was performed in these cases, with destruction of the root by avulsion. The authors felt that this was necessary because herpes zoster involved not only the ganglion and root but other deep centers and that avulsion of the root was much more efficacious. Complete cure resulted in all 3 cases. Wood, in 1929, described a case of zoster in a woman, who continued to have intense and constant pain on the left side of the face. He injected procaine into the supraorbital nerve just back of the foramen. Complete relief of pain followed. For this reason, he advised division of the supraorbital nerve just behind the foramen, pulling out as much of the proximal end of the nerve as possible to delay union. Cushing, in 1920, treated 3 patients with severe zoster neuralgia. In 1 trigeminal neurectomy was done, and in the other 2 the supraorbital nerve was avulsed. Halphen published a report of a case

with vesicular eruption of the left side of the face, edematous lids and violent pains. In view of the intensity and the persistence of the pain, and with knowledge of the theory of the sympathetic origin of facial pain, anesthesia of the sphenopalatine ganglion was induced, with injection of alcohol via the nasal route. The patient experienced immediate relief of pain. The herpetic vesicles dried up on the fourth day, and crusts fell off on the eighth day. Anesthesia of the sympathetic and of the superior maxillary nerve can be obtained by injection behind the tip of the middle turbinate bone. He asserted that disappearance of pain was due to the irritation of the ophthalmic nerve. This was explained on the assumption that the alcohol paralyzed the fibers of the sympathetic system, since the anesthesia affected only the fibers of the superior maxillary nerve, or that relief from pain was due to trigeminal anesthesia, entailing a vasomotor alteration locally or remotely in the region of the sympathetic, with relief of pain from this vasomotor alteration, such as results from action on the sphenopalatine ganglion. In many cases of trigeminal neuralgia, Frazier found that cocaine of the sphenopalatine ganglion controlled pain almost immediately. He concluded that the treatment paralyzed the sympathetic fibers. Kowler, in 1937, reported good results in 2 cases by painting the entire middle turbinate with a solution of Bonain, phenolized cocaine.

Freidenwald, in 1929, was the first to use convalescent serum in this disease, with immediate relief of pain. The cutaneous rash rapidly subsided. McDonald, and Walker and Walker reported good results with this serum. Gunderesen, in 1940, gave detailed observations and reported on 91 patients so treated. Sixty-one (66 per cent) had ocular infection, and of these, 82 per cent had useful vision. Of his patients not treated with any specific remedy, 40 per cent had useful vision. He claimed that good results may be expected if treatment is given before the ocular infection is established, especially during the first few days following the eruption. The treatment not only relieved the pain with startling suddenness but cut short the course of the disease. For those who prefer this type of treatment, convalescent blood or serum, for this disease, blood banks should be found to be useful. Cornil and Blanc, in 1931, reported on treatment of a patient with 20 cc of blood taken from a patient convalescing from zoster. Complete relief of pain followed at once.

The practice of autohemotherapy of dermatoses dates from 1913. It was preceded during three

years by hemoserotherapy, consisting in treatment of the patient with serum of a healthy person. In 1913, Ravault simplified the method of autoserotherapy by utilizing whole blood of the patient from a vein in the elbow. This was reinjected at once under the skin of the abdomen or into the muscles of the buttock. This treatment was used for various cutaneous diseases, including herpes zoster. Spillman and Raspiller, in 1923, used this method successfully in treatment of zoster, as did Pillsbury and Fonde, Parisot and Simonin, Avalos, Drouet and Vermeil, Wintzer, Beeson, Wagner, Resmond, Terrien, Barrio de Medina, Barksdale, Worms, Sourdille and Legrand and Francois. This treatment consists in withdrawal of 5 to 20 cc of blood and its injection into the patient's gluteal muscles. The amount of blood varies. Children are given half of the amount for adults. There are no after-effects except slight pain at the site of injection, and in some cases a mild febrile reaction ensues. As a rule, two or three injections suffice. There are usually rapid relief of pain and healing of the vesicles. Drouet used this method in 8 cases of ophthalmic zoster, with excellent results. Even with the initial injections, almost complete disappearance of pain resulted, with rapid attenuation of eruptive symptoms. The vesicles became desiccated in two or three days, and the zoster was cured in ten days. The neuralgias were never observed to return after the treatment. In 1 of his cases there were three recurrences without specific treatment, but after the autohemotherapy the symptoms disappeared and there were no more recurrences. Sédan gave eight injections to each patient. The first injection was of 5 cc, the second and third, of 10 cc each, the fourth of 15 cc, the fifth, of 20 cc, and the sixth, seventh and eighth, of 30 cc each. All treatments were given at intervals of three days. Sédan concluded that a subnormal tension of the globe almost always became elevated at the end of five or six hours but that on the following day it declined to a level lower than that noted prior to injection. Although the mechanism of the action is still obscure, it is probably that of a protein shock produced by albuminoid substances of the blood. Wintzer asserted that the action was based on sensibilization and desensibilization. Paillard stated the belief that the blood was slowly absorbed by the lymphatics and produced a favorable defense reaction. Spillman and Raspiller expressed the belief that the treatment could be classed with the methods of nonspecific desensibilization.

I have used this method with success in several cases. The procedure is simple, and pain is

quickly relieved. The eruption responds to treatment, and few injections are necessary. Early treatment prevents severe pain and ocular complications. It has no effect on well established uveitis, due to zoster, but it may prevent development of new uveal foci of infection. During the eruptive period when palpebral edema is present, local treatment should be restricted to moist compresses to avoid accumulation of secretion. In some cases the lesions of the skin are best treated with a mild astringent lotion, such as solution of calcium hydroxide twice daily. Olive oil is often of benefit in cleansing the skin. At times a protective dressing is necessary. Cold air and drafts should be avoided. Ten grains (0.65 Gm.) of acetylsalicylic acid every four hours will usually relieve pain, but in some cases morphine is necessary. Atropine and ethylmorphine hydrochloride may be indicated if the cornea or the iris is involved. Tetracaine or some other useful local anesthetic may be advisable for the relief of pain in the cornea or the conjunctiva. Mild protein silver, neo-silvol or some other preparation of silver is often found to be useful.

As soon as swelling of the lids subsides and the affected eye can be opened, an examination for corneal anesthesia should be conducted, and afterward tests for the extrinsic and intrinsic motility of the globe should be made. While corneal anesthesia persists, the eye should be covered with an occlusion bandage and if anesthesia or corneal ulceration persists, tarsorrhaphy should be performed and the suture maintained for several weeks.

Even after the disappearance of zoster, patients should remain under observation, since corneal disturbances or increase of tension may manifest itself at a late date and disturbance of sensibility may persist for a long time, and perhaps indefinitely.

### CONCLUSIONS

The severity and duration of the disease vary. Complete recovery may follow in a few weeks, or the condition may drag on for months in spite of treatment. In all cases of herpes zoster there is a morbid condition of the sensory nerves supplying the affected area, and the type and localization of the changes are variable. Specific clinical manifestations appear to be the result of some form of irritative reaction to the ganglion or nerve whether due to infection, trauma or intoxication. It may be that predisposing factors favor the establishment of herpes zoster, such as cold injury, head colds, specific infections or sinus or dental disease. The process may start in various portions of the nerve, the ganglion or

the peripheral branches, and even in the contiguous ganglions connected with the nerve, such as the sphenopalatine ganglion in the case of the fifth nerve.

In a vast majority of cases of ophthalmic zoster the disease is secondary or symptomatic. The causes and character of the basic disturbance vary. Different kinds of systemic disease, even latent ones may result in herpes zoster ophthalmicus. The basic disease may even run its course, leaving only a predisposition to nervous disturbance or nervous irritability. Levaditi stated his belief that various causes were provocative agents, forming a place of least resistance on which the latent virus of zoster might act.

It is not known whether in cases of herpes zoster which occurs coincidentally with other infectious diseases the zoster is actually produced by the same etiologic agent or whether it is produced by its own virus, the infection being facilitated by general lowering of bodily resistance.

According to some authorities, spread of the virus occurs through the cerebrospinal fluid, and thus it is explained how the more superficial fibers originating from specific sensory nerves or fibers destined for certain muscles are first affected in certain ganglions or nerve trunks. Proponents of this theory regard ophthalmic zoster as a manifestation of various infectious processes, which are spread by way of the spinal fluid, and so account for its selective action on particular sensory filaments and muscles, whose nerve fibers are superficially located in the nerve trunk, which is bathed by the fluid. Goeckerman and Wilhelm stated the belief that the same lesion might result from several causes, including trauma, hemorrhage and focal infection. They were not convinced that a single agent caused the disease.

There may be a form of zoster not induced by neuritis or inflammation of the nerve ganglions but due to a disturbance in the higher sensory centers of the trigeminus in the medulla oblongata (bulbar type), which has to date been described in 1 case, in which malaria was the cause, by Daring and Huber. In this case, they concluded that the seat of trouble was a paralysis of the bulbar nuclei, probably located where the centers of the sensory trigeminus and the vagus nerve and the posterior horns of the second and third cervical segments lie close together. They stated the belief that in this case the zoster was due to a vascular alteration after malaria, following endothelial proliferation and partial occlusion of vessels.

The traumatic origin of the disease has never been scientifically demonstrated, although it is possible that there is a connection between corneal trauma and corneal herpes zoster. In these cases, it is questionable whether injury is the prime etiologic factor.

Ocular paralyses which supervene during the course of zoster are not so rare as is generally assumed, although their frequency is variously estimated by different observers. Their occurrence is independent of the intensity and distribution of the eruption. They usually occur two or three weeks after the eruption. The third nerve is most frequently involved, and the paralysis may be partial or total. It may be revealed by ptosis or mydriasis, although it must be remembered that these conditions may also be produced by inflammatory ptosis, or by alteration of the pupil due to lesions of the cornea, or by paralysis of the sympathetic fibers. It has been demonstrated by Ingvar that the fibers corresponding to the levator palpebrae and the superior rectus muscle occupy a superficial situation in the dorsal part of the nerve trunk of the fifth nerve, while those corresponding to the inferior oblique muscle are also situated superficially but in the ventral part. Therefore, these muscles would be more readily affected by pathogenic agents attacking the nerve trunks externally, as in instances of basal meningitis or in cases in which the infectious agent is spread by the spinal fluid.

Combinations of paralysis of the trochlear and the abducens nerve sometimes occur. Only 2 cases of bilateral paralysis have been noted in the literature, 1 of the sixth nerve, reported by De River, in 1926, and the other, of the third nerve, reported by Gallois, in 1924. Paralysis of the motor nerves of the eye may be due to extension of the disease to the trigeminus and then to the motor nerves by way of the sensory ramifications, which the first branch of the fifth nerve sends out to all motor nerves of the eye, before entering the orbit. Vernon stated the belief that paralysis of the ocular muscles was due to the same influence as the herpes, and Wyss was inclined to refer the muscular paralysis to myositis. I found 242 cases of paralysis of the ocular muscles in the literature.

The lacrimal gland reveals its participation in the disorder by disturbances of nerves controlling the secretion of tears, which cause abundant transitory lacrimation. Terrien said that the keratitis was favored by the abolition of continuous lacrimation, which he thought depended on the facial nerve, and stated that when the petrous bone was removed at the same time as the ganglion, the secretion of tears disappeared and the

cornea was altered. But if the ganglion was sectioned without cutting out the petrous bone, the secretion of tears was preserved.

The epithelium of the cornea is soft, delicate and loosely attached to Bowman's membrane. It is liable to injury, has a precarious nutrition and retains its health mainly through its sensitiveness. The fifth nerve supply protects the cornea by the sensation of pain and by the trophic influence, the influence which the healthy nerve has on corneal nutrition. This case of epithelial denudation is an important factor in development of corneal disorders. In herpes zoster there is corneal anesthesia, and this invites secondary infection and renders the cornea liable to injury. In addition, there may be an irritative influence passing down the nerve, causing disturbed nutrition, or the normal influence that passes along the nerve may be disturbed. In addition to the detached corneal epithelium, the small, inflamed terminal nerve fibers set up an irritative process at the periphery. In cases of corneal ulceration, the result is that characteristic of every infection of the cornea. The lesion may terminate in a scar and leave a serious diminution of vision.

The fifth nerve is similar, morphologically and physiologically, to the posterior radicle of a spinal nerve. According to Talkovskiy, it has a definite biologic arrangement in the ectodermal portion of the cornea and appears to be neurotropic for an ectodermal virus. He claimed that the development of the corneal process was explained by the morphologic character of the nerve apparatus of the cornea, the status of the nerve portions and the anatomic communications with the nerve network of the cornea.

There is always anesthesia with zoster of the skin, and usually areas of anesthesia are found on the cornea. The cornea may be hypesthetic, and some authors believe this loss of sensation underlies the corneal lesions. Experimental work has shown that in cases of section of the trigeminus in which sensibility was preserved keratitis was rare, while keratitis was present in the majority of instances in which anesthesia was absolute. The impairment of corneal sensation varies, the degree depending on the amount of damage sustained by the ganglion. Head and Campbell showed in their researches that the more severe keratitis was associated with complete destruction of nerve cells in the ganglion. Lesions of the cornea are present in 40 per cent of cases.

Various hypotheses are given to account for the optic neuritis. Included among these are reflex disturbances, particularly the anastomotic union of a filament of the ciliary nerve with the optic nerve, accompanying the central artery of

the retina. According to this theory, infection proceeding from the ganglion descends along the trunk of the ophthalmic nerve and thus reaches the optic nerve.

Iritis often manifests itself as an anterior uveitis or an iridochoroiditis and is characterized by its torpidity and by the minute peripapillates on the posterior surface of the cornea. In some cases, the classic form with posterior synechias is seen. It may be associated with hypertonia, even though iritis is ordinarily associated with hypotonia. Iritis is present in about one fifth of all cases of ophthalmic zoster.

No definite etiologic factor has been found. Some kind of acute intoxication takes place, becoming localized in the ganglion and producing a toxic element that irritates the nerve ends of the part involved, causing herpes to develop. It is questionable whether the disease is due to any special etiologic factor, even though it appears contagious at times.

The cutaneous lesions may be due to products of degenerated ganglion cells conveyed along the nerve to the termination in the skin or to the exciting organism itself acting through nerve impulses on actual passage of the virus, or to the products of degenerated nerve fibers in the skin. There is selectivity, for at times the skin is not even reddened between the vesicles, and the vesicles do not appear in all parts of the skin supplied by the nerve.

Whether the disease is due to selective affinity of some virus or bacterium in a focal lesion, as claimed by Rosenow, or to the selective action of their toxins, as suggested by Mackenzie, is questionable. If one virus is responsible for so many different lesions, it is certain that it is capable of different action at various times and places. It is quite possible that the virus is liable to a variable virulence and may be inconstant in its affinity for the bipolar ganglion cells. Irritation of these cells causes the herpetic eruption, whether due to a virus or to some inflammatory process or growth. Whether it is exogenous and extends to the ganglion by way of the nerve, or whether it is endogenous and is attracted by the nerves and ganglion through increased neural irritation is not known.

Age and sex are not factors. On the basis of findings in the blood in the disease and of reports in the literature, the infection is thought to be of low virulence, and no definite conclusion can be drawn concerning the severity of the disease by examination of the blood.

The disease is often associated with dental and focal infection, but most adults have enough in-

fection, local or general, in their systems so that an attack could occur at any time and need not appear in epidemic form. There may be a special local or general susceptibility, for not every one has the disease.

The essential cause of the disturbance is unknown, whether destruction of trophic fibers, irritation of nerve elements, injury to insensitive structures, spread of the degeneration process from nerve terminals to cells in the ganglion or a specific infection.

The pathologic process of ophthalmic zoster is a disturbance either in the gasserian ganglion or along the course of the branches of the fifth nerve or both, affecting the skin, mucous membranes and tissues supplied by these nerves. These lesions may be the result of hemorrhage in the ganglions or the sheath of the nerve, causing pressure on the nerve, or of senile degeneration or a localized inflammatory process in either the nerve or the ganglion, or a tissue reaction to various types of irritant.

Secondary degeneration may be found in the posterior columns of the cord, in the fibers of the posterior roots central to the ganglions and in the afferent fibers of peripheral nerves leading to the ganglions.

In consequence of observations and experiments by many investigators, most writers conclude that an independent pathologic entity is involved and that herpes zoster is an infectious disease of one or more spinal ganglions.

It is possible that, instead of a virus, the real nature of the cause is a change in complex protein molecules. Different strains or different arrangements of the molecule may produce various types of disease. The molecule under different degrees of body temperature may become weakened or strengthened to such an extent that it can then enter the body cells, which have been altered, and the molecule is then capable of producing a different disease, such as herpes zoster or varicella. Investigators have shown that the molecule can grow when it touches the exact kind of living cell it likes for a home. These nonliving molecules, or enzymes, merely exist, neither growing nor dying. They move about when they enter certain cells and then grow, and probably reproduce. If their structure is unchanged, they are harmless, and the way in which they are put together determines whether or not they are dangerous. The molecule is at the mercy of its environment, but on entering the right kind of cell, it reproduces itself and grows. As a result, rapid growth of molecules may cause immediate death of the cell. It was not



until the development of the electron microscope that viruses could be photographed and their structure studied, and in all probability a virus is a protein molecule

After having made an exhaustive search of the literature, and with the aid of several translators, I find that there are approximately 2,250 cases of ophthalmic zoster reported to date. Some investigators have made a very careful study of cases and of the pathologic changes and the picture presented. Others have made only brief reports, with short case histories. In many of the cases described there was no reference to sex or age or to the eye involved. The average age was found to be 43 years, males were affected in 54 per cent of the cases, the right eye was involved in 54 per cent. The cornea was disturbed in 39 per cent and the globe affected in 49 per cent. The ocular muscles were involved during the disease in 13 per cent of cases and the facial nerve in 7 per cent. An Argyll Robertson pupil was described in 23 instances, and glaucoma appeared in the course of the disease in 65 cases. There were reports of 35 cases of episcleritis, 41 cases of recurrent ophthalmic zoster and 52 cases of the bilateral disease. All the branches of the fifth nerve were involved in 25 cases, and the first and second branches were affected in 67 cases. Retrobulbar neuritis, optic neuritis and optic atrophy appeared in 40 cases, and in numerous cases perforation of the globe resulted from panophthalmitis. In 68 cases of ophthalmic zoster the patient was under 20 years of age, in 44 cases, under 13 years, in 24 cases, under 6 years, and in 14 cases under 1 year of age.

#### REPORT OF PERSONAL CASES

J. C., a man aged 75, complained of severe pain over the right eye and the right side of the head one day after being exposed to a cold wind and rain. The neuralgic pain was of sudden onset in the area of distribution of the first branch of the fifth nerve, followed in two days by a vesicular eruption.

He was seen two days after the eruption, which appeared on the right side of the forehead, sharply demarcated against the midline and extending to the scalp, eyebrow and external palpebral commissure. There was associated edema of the conjunctiva, which partly covered the cornea, with increased lacrimation. Vision at this time was 20/100 in the right eye and 20/20 in the left eye. The temperature was 37.5 C (99.5 F), the respiratory rate 20 and the pulse rate 90 a minute. The white cell count was 10,000. The urine was normal, and the Wassermann reactions of the blood and the spinal fluid were negative. The personal history was noncontributory. The patient was a well developed, well nourished, healthy man. The heart was normal in size, rate and rhythm. No murmurs were present. The blood pressure was 160 systolic and 80 diastolic. The lungs were clear on percussion and auscultation, and no rales were present.

The abdomen showed no tenderness or palpable masses. The reflexes were normal.

Four days later sudden diplopia appeared, due to paralysis of the right sixth nerve. There were simultaneous increase in the periorbital edema and the appearance of a new crop of vesicles at the nasal angle of the right eye and over the right half of the nose, in the area supplied by the infratrochlear nerve. The eyeball became intensely injected, with much lacrimation and mucopurulent discharge. The ocular tension was increased. A few erosions were noted on the cornea, which was somewhat edematous and hazy. The corneal infiltrate involved most of the nasal half of the cornea, with some vascularization. Hyperesthesia of the skin was present in the area supplied by the fifth nerve. The cornea was insensitive.

The paralysis of the abducens nerve coincided with the appearance of the secondary crop of vesicles at the nasal angle of the right eye, probably the result of the direct extension from the nasociliary nerve to the sixth nerve in their passage through the supra-orbital foramen or deeper in the orbit.

The cutaneous eruption went through the stages of vesicle formation, drying of pustules, crusting and pigmented scarring. The acute phase of the infection subsided in about eight weeks, and sixteen weeks later all symptoms had disappeared. The resulting vision was 20/60. All diplopia disappeared in two weeks and the tension returned to normal.

The pupil was kept dilated with 1 per cent atropine sulfate, and 10 per cent neo-silvol was used in the eye three times daily. The eye was kept covered. Salicylates were administered freely for the relief of pain. Calamine lotion was used for the lesions of the skin. Thiamine hydrochloride, 2,000 units, was given daily for six days.

CASE 2—E. R., a man aged 40, after a few days of general malaise, headache and pain in the left supra-orbital region, presented typical herpes zoster of the first branch of the left trigeminal nerve. When he was first seen, there was an eruption of vesicles, some dried and crusted, on the left upper lid and the left side of the forehead and nose, sharply limited to the midline. The lid was edematous and heavy, with chemosis of the bulbar conjunctiva. There was no proptosis or immobility of the globe. The cornea was hazy, with small areas of ulceration and a definite ciliary flush. The pupil was moderately dilated. The ocular tension was normal. No details of the fundus could be seen.

The temperature was 37.5 C (99.5 F), the white blood cell count was 9,500, the urine was normal, and the Wassermann reactions of the blood and spinal fluid were negative.

His sight had always been good in each eye, and there was no history of any previous ocular trouble. His general health was excellent. Examination of the heart and lungs did not reveal any abnormality or evidence of disease. The abdomen showed no areas of tenderness.

Atropine was used to dilate the pupil, and local supportive measures were administered. Autohemotherapy, with injection of 10 cc, was used and the injection repeated two days later. Immediate cessation of pain followed, and definite improvement was noted in the cutaneous eruption.

Three weeks later the corneal involvement had disappeared, with no remaining leukoma. Vision was normal in each eye. The pupil was round and reacted normally to light, in accommodation and consensually.



The fundus showed no abnormality. There was no subjective or objective evidence of disturbed equilibrium of the ocular muscles. Vision was 20/30.

CASE 3—C G, a man aged 45, complained of severe pain and inflammation of the left eye. Neuralgia persisted, and soon there was swelling over the left temporal region, the lids became swollen and closed. The next day many small, yellow, raised and irregular blisters appeared on the left side of the nose, the upper and lower lids of the left eye and the skin of the left frontal region as far as the hair line. These vesicles were absent from the remainder of the face and were definitely delimited by the median line, so that they occupied the left side of affected regions exclusively. The conjunctiva was decidedly hyperemic and chemotic. The cornea showed several small, pinhead erosions. The pupil was dilated, and the iris was free. Ocular tension was not increased. The preauricular and posterior cervical glands were enlarged.

The temperature was 37 C (98.6 F), the pulse rate was 78 a minute. The white cell count was 11,950, and the red cells were increased to 5,720,000. The urine showed an excess of albumin. The Wassermann reaction was negative. The results of the general physical examination were essentially normal. His health had always been good, and there was no history of any previous trouble with the eyes.

On the sixteenth day diplopia developed, due to paralysis of the left sixth nerve, which in two weeks had disappeared. At the end of the third week the corneal disturbances had also disappeared, with regeneration of corneal epithelium. Some superficial vessels were noted at the nasal limbus of the cornea. Vision was 20/40.

At this time the vesicles of the skin had dried and formed thick, yellow-brown crusts, which fell off, leaving deep pits in the skin. Complete anesthesia persisted and extended to the scalp.

In this case the first and second branches of the left fifth nerve were affected. No specific treatment was administered. Atropine was used in the left eye as soon as the corneal condition was noted. Neosilvol, 10 per cent, was instilled in the eye three times a day, and the eye was kept closed. Calamine lotion was used on the surface of the skin. Acetylsalicylic acid was given freely for the relief of pain.

CASE 4—P F, a man aged 62, complained of severe pain over the right eye, which extended up and back over the frontal and the parietal region. This pain lasted for forty-eight hours and was much increased during each night. The right upper lid was swollen and heavy, causing the eye to close. By lifting the lid, however, he could see that his vision was not affected. The pain he described as an "intermittent lightning pain," from which he was not free at any time. The neuralgia later extended down the right side of his nose. At this time, on the fifth day, vesicles appeared over the painful region, to the right of the midline. The pain lessened but did not disappear. The vesicles were clear, extending over the frontal region into the scalp and along the right side of the nose to the tip. On the right brow was a large, linear vesicle. Two vesicles appeared on the upper right lid. The eye was intensely engorged, with much lacrimation and photophobia. Some conjunctival discharge was present. Several small vesicles appeared on the cornea, and vision was greatly reduced. These vesicles occupied most of the pupillary area of the anesthetic cornea. Part of the iris could be seen and appeared swollen. The pupil was indistinct but of medium size and was

not quite round. No details of the fundus could be seen. The preauricular glands were enlarged. The heart and lungs showed no evidence of disease. The blood pressure was 140 systolic and 75 diastolic. The abdomen showed no areas of tenderness.

Atropine was used as soon as the cornea was involved. Part of the iris remained fixed and swollen, and the vessels of the iris were easily seen. Tension remained normal. Autohemotherapy, with injection of 10 cc, was used and the injection repeated twice, on alternate days. Calamine lotion was used on the cutaneous lesions. On the fifth day all pain had vanished, and the cutaneous eruption was vastly improved. The crusts of the skin loosened, leaving deep scars corresponding to the confluent group of vesicles.

Examination with the slit lamp showed small opacities in the deeper corneal layers, with deposits on Descemet's membrane. After staining with fluorescein, the minute corneal defects could be seen to greater advantage. The iris showed atrophy and appeared a duller tint than the iris of the other eye. It had lost its areolar structure, some crypts were effaced, and the fibrils were blurred. A few pigmentary spots were noted on the anterior capsule.

The white cell count was 8,100, and the red cell count was 4,850,000. The urine was normal, and the Wassermann reactions were negative.

Six weeks later the ocular condition was quiet, with a central corneal leukoma remaining. At this time he suffered severe pain in the right eye, and two days later there appeared some ciliary injection and a hazy area was noted below the cornea. A small nodule of violet-slate color developed, with marked injection of vessels at this point, this nodule became a small vesicle on one of the anterior ciliary nerves, resembling an area of episcleritis. Atropine sulfate, 1 per cent, was again used in the eye, and the pupil was kept in a state of dilatation. The eye was kept covered. Sodium salicylate, 10 cc, was given three times a day until all pain and discomfort disappeared. Weeks later the conjunctiva recovered its normal condition, and the nodule was less pronounced, appearing of a grayish tint. Four weeks later the nodule had disappeared, and in its place was a small darkened discoloration of the sclera. This nodule was beneath the conjunctiva and near the limbus but did not touch the cornea. One year later vision was 20/30 with correction.

CASE 5—Mrs T T, aged 70, was first seen five days after the outbreak of herpes zoster. A number of vesicles were noted on the left upper lid and the forehead, scalp and tip of the nose on the left side. There was intense ocular congestion with a central corneal ulcer. Severe neuralgic pain was present over the area involved, and from the upper left lid to the scalp the skin was red and tender, with swelling of the preauricular glands.

Vision was greatly reduced. The temperature was 38 C (100.4 F). The urine was normal, and the Wassermann reactions of the blood and spinal fluid were negative. The red cell count was 3,750,000 and the white cell count 10,000. The differential count showed 41 per cent polymorphonuclears, 30 per cent eosinophils, 22 per cent small lymphocytes, 5 per cent large lymphocytes and 1 per cent basophils. The hemoglobin concentration was 84 per cent. The general physical examination did not contribute anything pertinent to the case. There was a history of exposure to chickenpox, three weeks before her present illness.

Ten cubic centimeters of blood was withdrawn from the arms and injected into the gluteal region (auto-

hemotherapy) This was repeated two days later After four days there was complete cessation of the pain, and the cutaneous condition was much improved and the eruption had mostly disappeared This treatment, however, did not seem to have any effect on the corneal condition Atropine was used to keep the pupil dilated Codeine was used for relief of the pain, and calamine lotion was used over the skin of the forehead and the scalp

About four weeks after the onset the edema of the lid had subsided, and the patient was able to keep her eye open The eyeball was considerably injected throughout the illness, with much lacrimation and mucopurulent discharge The corneal ulcer had healed, but corneal sensation was still greatly diminished At this time there were noted many minute, gray papules in the cornea, and she complained of diplopia Examination showed this to be due to paresis of the left trochlear nerve

The pupil was round and measured 6 mm in diameter The fundus details were hazy Examination with the slit lamp revealed numberless minute gray spots situated in the epithelial layer of the cornea, in contact with Bowman's membrane These spots were more dense toward the center and more scattered at the periphery The superficial outline of the iris could be easily seen The pupillary margin was pigmented, and in places particles of pigment had become separated from the iris Two small holes were seen in the iris, which permitted light to pass through

For several months severe neuralgia remained in the left eye, left temple and scalp Cutaneous anesthesia was present The upper lid remained red and thickened, and the eyeball was injected for some time The conjunctival injection gradually subsided, and the skin of the upper lid and forehead was extremely tender to touch for a long time The corneal involvement gradually became less apparent The diplopia gradually became lessened and in one year had disappeared Vision was 20/30

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# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

## Conjunctiva

A CASE OF PRIMARY CHANCER OF THE BULBAR CONJUNCTIVA C DEE SHAPLAND, Brit J Ophth 28 187 (April) 1944

A man aged 20 complained of a discharge from the left eye of ten days' duration. There was edema of both lids and the caruncle and plica semilunaris were unduly evident. The parotid and submaxillary glands were firm and discrete. On eversion of the lower lid a band of cartilaginous consistence, directly continuous with the lower end of the edematous plica and laterally becoming lost on the bulbar conjunctiva inferotemporally, came into view. On its surface there was a small, grayish white ulcer, with sloughing base. There was practically no discharge. A specimen of serum from the ulcer contained *Treponema pallidum*. Serologic tests of the blood gave weakly positive reactions for syphilis. There was a gradual, almost complete, disappearance of all symptoms under treatment with oxophenarsine hydrochloride (mapharsen) and a proprietary suspension of metallic bismuth.

The article is illustrated with a photographic plate in color.

W ZENTMAYER

VIRUS OPHTHALMIA NEONATORUM A SORSBY, E E HOFFA and E N YOUNG, Brit J Ophth 28 451 (Sept) 1944

An account of the inclusion type of ophthalmia neonatorum is given. From a study of 27 cases observed in a series of 269 consecutive cases of ophthalmia neonatorum at White Oak Hospital it is concluded that, apart from a later onset in most, but by no means all, cases, inclusion blennorrhea has no features which distinguish it from microbial ophthalmia neonatorum, either in course or in response to sulfonamide therapy. In 5 of 25 mothers of infants with inclusion blennorrhea, cervical scrapings showed inclusion bodies.

The article is illustrated.

W ZENTMAYER

## Cornea and Sclera

DESICCATION KERATITIS J E M AYOUB Brit J Ophth 28 347 (July) 1944

The article describes a corneal disorder which was first noticed among the troops of the Eighth Army fighting in the desert during the summer of 1942. A private communication from Capt Martin Williamson, M C, R A M C, indicates that the condition was widespread and occurred

especially in observation post officers, drivers and patrols—all key men.

The subjective symptoms included smarting and itching of one or both eyes, profuse lacrimation, severe photophobia and definite disturbance of vision, which consisted either of unocular diplopia or of seeing dark objects as having a tail-like prolongation, like a comet, or as vaguely blurred.

Only the superficial epithelial layers of the cornea were affected. Three main types were noted. 1 The commonest lesion was a bandlike roughening of the corneal epithelium across the area which would be exposed when the eyes are partially closed, as is the case in a bright light. The band was grayish, but translucent, and stained with fluorescein, revealing the loss of epithelium. The appearance was punctate. 2 The lesion was sometimes limited to a few lines of grayish dots, mainly horizontal and in the exposed regions of the cornea. These dots also stained with fluorescein. 3 A single stippled line, actively staining, was also seen at times.

The fissural portion of the eyeball was congested. The following causative factors are discussed: (1) damage by light radiations of short wavelength, i.e., photophthalmia, (2) damage of the epithelium by driven sand, carried in a sandstorm or raised by vehicles driving in front or by shelling, (3) action of irritant gases, (4) drying of the exposed area of the cornea by intensely hot air or wind, (5) undue exposure of the affected area of the cornea due to fatigue, which reduces the frequency of the blinking reflex of the lids. This would predispose to the influence of factor 4. It is probable that the cause is drying of the corneal epithelium by a hot dry wind, which produces excessive evaporation of the lacrimal secretion over the exposed area of the cornea.

The suggestion is put forward that corneal damage ascribed to snow blindness is caused, certainly in part, by desiccation and perhaps also by freezing of the corneal epithelium, and not by excessive reflections of ultraviolet light.

W ZENTMAYER

DESICCATION KERATITIS J E M AYOUB Brit J Ophth 28 347 (July) 1944

A STUDY OF EIGHTY-FOUR CASES OF DELAYED MUSTARD GAS KERATITIS FITTED WITH CONTACT LENSES I MANN, Brit J Ophth 28 441 (Sept) 1944

Mann gives the following summary. Eighty-four cases of delayed mustard gas keratitis are reviewed. All the patients were fitted with contact lenses some of them seven years ago. Thirty-

nine of the patients wear their lenses from eight to sixteen hours a day, 11, from five to eight hours, 8, under five hours, 5, not at all, and for 21 the time is not known. The visual acuity of all but 2 patients was notably improved. In 25 cases there was no further relapse after fitting, in 4 cases there was one relapse only, in 16, slight relapses, and in 10 only were the relapses severe. The age of onset of the symptoms, the occupation of the patients and the treatment of intercurrent complications are discussed.

W ZENTMAYER

HERPES SIMPLEX CORNEAE IN MALARIA J  
GRAHAM SCOTT Brit M J 2:213 (Aug  
12) 1944

In 4 cases of unocular herpes simplex corneae among 4,000 cases of malignant tertian malaria corneal lesions occurred between the seventh and the sixteenth day of illness. The best result followed removal of the corneal epithelium with a strong iodine solution (7 per cent iodine and 5 per cent potassium iodide in alcoholic solution).

ARNOLD KNAPP

TREATMENT OF CORNEAL DISEASES BY RIBO-  
FLAVIN S BARRENECHEA, R CONTARDO  
and J ARENTSEN, Ophth ibero-am 4:405,  
1943

Barrenechea and his associates treated with riboflavin 109 patients presenting corneal ulcers and corneal vascularization of various causes. In 70 per cent of the patients the disappearance of ulcers and vascularizations was remarkably rapid. The average time for the complete healing of the ulcers was seventy hours. The vascularization disappeared in three days to two weeks. The treatment failed with 30 per cent of the patients, 15 per cent of whom were shown to have tuberculous ulcers, which flared up on the administration of riboflavin.

J A M A (W ZENTMAYER)

### General Diseases

REPORT ON TWO PAIRS OF BROTHERS SHOWING  
MARFAN'S SYNDROME H J STERN, Brit  
J Ophth 28:229 (May) 1944

The oldest brother of the first pair was 14½ years of age, underweight and undeveloped, he showed hypogonadism, an undescended right testicle and a small left testicle. There were frequent extrasystoles and prominent hypertrophied veins on the chest. The limbs and fingers were characteristic of the syndrome. There was incomplete embryotoxon. The pupils were irregular in shape, and there was iridodonesis. There were two small bridge colobomas of the iris. In its temporal lower part the iris showed

a peculiar spongy structure, making the parenchyma partly float in the anterior chamber. Both lenses were luxated. The sella turcica was very small.

The younger brother was 12 years of age. He was undersized. Arachnodactyly was present. Both lenses were displaced.

The parents were healthy and normal. The sella turcica of the father was small.

The parents and other children of the second pair of brothers suffered with more or less severe obesity of endocrine origin. Several members of the family had high myopia.

The older brother was 14 years of age and was oversized but well developed. Arachnodactyly was present. There was habitual subluxation of the humerus and of the fingers. The sella turcica was small. There was subluxation of both lenses.

The younger brother was 11 years of age. He was oversized. He presented the same general anomalies as his brother. Both lenses were subluxated.

The author believes the 4 cases presented support the views expressed by Mann that the disturbances in Marfan's syndrome are probably only coordinated symptoms of a genotypic disturbance, producing general and ocular troubles which affect not only the mesoderm but the endocrine glands and the ectoderm.

W ZENTMAYER

### Injuries

THE EYE DEPARTMENT IN A MIDDLE EAST GEN-  
ERAL HOSPITAL H B STALLARD, Brit J  
Ophth 28:261 (June) 1944

The author gives a brief survey of the organization and nature of the work of the department of ophthalmology in one of the hospitals serving in the Eighth Army from the autumn of 1940 to the conclusion of the North African campaign, in May 1943.

About 30 per cent of fragments from shells, hand grenades and land mines may be extracted by the posterior route. The figures for extraction of pieces from shells and land mines by the anterior route are less favorable.

Sixty-eight patients with retinal detachment were treated with surface diathermy and suction drainage of the interretinal fluid through diathermy penetration of the sclera and choroid. Three patients were treated for myopia, all successfully, 10, for cystic degenerations, all successfully, 20, for degeneration after healed choroidoretinitis, all successfully, 21, for contusions of civil type, with 18 successes, 2 immediate failures and 1 partial recurrence, and 18, for war trauma, with 14 successes and 4 partial recurrences.

W ZENTMAYER



BLIND BULLET INJURY TO THE EYE REPORT OF  
A CASE K U KAZANDASHEV, Vestnik oftal  
22: 48, 1943

A soldier was injured while lying on the ground shooting with his right eye open. There was chemosis of the conjunctiva, with pronounced exophthalmos and limitation of motion of the eyeball in all directions. A small entrance wound was present in the upper nasal quadrant of the conjunctiva, the iris was inflamed, and a number of hemorrhages were seen in the choroid and the retina. Vision was reduced to counting fingers. The roentgenogram showed a bullet in the orbit.

An incision was made in the brow, the orbital bone was removed, and the bullet was extracted from the muscle funnel. The inflammatory process in the eye became quiescent, and vision increased slightly.

The interesting feature of this case is that the bullet hit the eye directly but did not injure the eyeball or the orbital bones. The changes in the eye were of contusive character.

O SITCHEVSKA

### Methods of Examination

PRINCIPLES OF RETINOSCOPY PRESENTED ON  
BASIS OF THEORY OF PROJECTION M  
KLEIN, Brit J Ophth 28 157 (April)  
1944

The principles of retinoscopy are presented on the basis of the theory of projection. Klein gives the following summary.

The nature of the light pencil emitted by the patient's eye during retinoscopic examination is best understood on the basis of the projection theory.

Retinoscopy is an aperture test by means of which the point of reversal of a myopic eye, or of an eye made myopic by trial lenses, is determined.

The elements of the illumination and of the returning observation systems of retinoscopy are analyzed.

Certain factors need further consideration.

1 The retinoscopic field can be substituted by the mirror hole.

2 The speed of reflex movement is explained by the area of the cross section of the emitted light pencil at the plane of the retinoscopic mirror.

3 The brightness of the pupillary light depends on brightness of the light source, distance, apertures, loss in transmission and the vergence of the emitted light pencil.

4 The retinoscopic reflex seen in the pupil is influenced by the size of the original source of light and the mirror used.

5 The following factors influence the point of reversal. (a) Sudden change of light and

shadow at the point of reversal. (b) The observer's retina receives during the retinoscopic test image elements of the patient's fundus or confusion circles of it, depending on the vergence of the emitted light pencil. The size of the confusion circles is maximum at the point of reversal. (c) The factors influencing the point of reversal set a limit to the accuracy of retinoscopy.

A number of diagrams illustrate the optical principles involved. W ZENTMAYER

RETINOSCOPY IN ASTIGMATISM M KLEIN,  
Brit J Ophth 28 205 (May) 1944

Klein summarizes his results as follows.

"A table of the optical power of obliquely crossed cylinders, and the implications of oblique cylinder ideas for retinoscopy with cylinders are presented.

"The basis of streak-retinoscopy is a band-like retinal image of the immediate source of light, which can be rotated in the principal meridians of astigmatism.

"Similarities exist between cylinder-retinoscopy and streak-retinoscopy as regards ascertaining the axis and the amount of the required cylinder.

"A survey of different instruments of the streak retinoscope group, and their practical use is given." W ZENTMAYER

### Neurology

SIMPLE ATROPHY OF THE OPTIC DISK A SIGN  
OF SUBTENTORIAL TUMOR M PUIG So-  
LANES, Gac med de Mexico 73 199 (June-  
Aug) 1943

Puig Solanes directs attention to the diagnostic value of simple atrophy of the optic disk in cases of tumors of the fourth ventricle or of the cerebellum. Optic nerve atrophy in these cases is the result of the acute dilatation of the ventricular system. Because ventriculography is contraindicated in certain cases of cerebral tumor, the diagnostic value of simple atrophy of the optic disk is obvious. The presence of this change in patients with symptoms of intracranial hypertension and other signs of involvement of cerebral structures in the posterior cranial fossa is pathognomonic of a tumor in this area. The diagnostic value of simple atrophy of the optic disk in cases of the aforementioned conditions is so reliable that it renders ventriculographic examination unnecessary. The author reports 4 cases in which the diagnosis was verified by removal of the tumor from either the fourth ventricle or the cerebellum.

J A M A (W ZENTMAYER)

## Ocular Muscles

NORMS OF LATENT STRABISMUS IN SELECTION OF CANDIDATES FOR AVIATION SCHOOLS S M KHAYUTIN, *Vestnik oftal* 16:148, 1940

This study was made in order to evaluate the relation between horizontal heterophoria for distance and other functions of the eye. Examinations were made mostly in the afternoon, determinations of visual acuity, refraction, visual fields, muscle balance, accommodation, and color sense were usually made and an ophthalmoscopic study done. The Maddox scale and Maddox rod with prisms were used for the measurement of muscle balance. Of 1,500 subjects examined, orthophoria was found in 38 per cent, esophoria in 32 per cent and exophoria in 30 per cent. The ages ranged from 20 to 22 years, and visual acuity was not less than 0.8, in other words, there were few cases of myopia or astigmatism. In some of the subjects examined repeatedly during a period of eight to ten months, orthophoria changed into exophoria or esophoria. Fever and emotional stress produce heterophoria of 3 to 4 degrees.

The relation between muscle balance and depth perception was studied in 112 candidates by the Howard-Dolman apparatus. Heterophoria for distance of about 4 degrees does not affect depth perception.

The author drew the following conclusions:

1 That part of heterophoria which has no direct relation to anatomic causes is unstable, its amplitude depends on the refraction, the tonus of the muscles and the general physical and emotional condition.

2 Muscular asthenopia is not directly the result of heterophoria and depends not only on the tonus of the muscles but on the general condition.

3 With heterophoria up to 4 degrees the depth of perception does not deviate from the normal.

4 In cases of variation in the degree of heterophoria the tests should be repeated in order to eliminate accidental factors.

O SITCHEVSKA

## Operations

OPHTHALMIC SURGERY IN WARTIME A I POKROWSKY, *Vestnik oftal* 22:4, 1943

*Transplantation of Fat in Operations on the Lids*—Transplantation of fat in plastic operations on the lid is indicated (a) in cases of deep scars with adhesions to the bone, in which the skin is little traumatized and is not shortened too much, (b) in cases of scars of the bone with formation of fistula and (c) in cases of transplantation of skin in which irregular relief of the skin develops and disfigures the face. The histories of 4 cases in which fat was taken from the patient's body and transplanted under the skin

of the deep scar after injury to the lid and adjacent parts, so common in the present war, illustrate the good cosmetic results obtained in young persons with such injuries.

*Transplantation of Fat in Operations on the Injured Orbit*—Transplantation of fat is indicated in cases of injury or tumor of the orbit, the walls of which are either destroyed or thinned. Depressions may form, with resultant disfigurement of the face. The procedure is also indicated in cases of deformity of the conjunctival sac. The transplantation of fat in the orbit took completely in all but 4 to 5 per cent of cases. The operation should be done after the inflammatory process has quieted down, the fat is taken from the abdomen or the buttocks.

*War Injuries of the Lids, Early Plastic and Orthopedic Treatment of the Conjunctival Sac*—In injuries of the lids in wartime, Pokrowsky recommends the immediate use of sutures, which will avert the necessity of complicated plastic operations in the future. He believes that there may be local immunity to various micro-organisms, as infection is rarely encountered in suturing the lid despite the presence of a number of bacteria.

In injuries of the eyeball, including the lids and conjunctiva, Pokrowsky advises that necessary surgical procedures on the conjunctival sac be done immediately after the enucleation, as the conjunctiva does not easily become infected and does not shrink much. In order to enlarge the conjunctival sac, a deep incision of the conjunctiva is made parallel to the margin of the lid, a prosthesis is used systematically after cod liver ointment is applied, and thus the conjunctival sac retains its normal size. The author illustrates the case histories. He stresses that each case be individualized in order to restore the normal relation of the tissues.

O SITCHEVSKA

## Orbit, Eyeball and Accessory Sinuses

INCOMPLETE AVULSION OF THE EYE REPORT OF A CASE I C MICHAELSON, *Brit J Ophth* 28:458 (Sept) 1944

The patient was a man aged 29 years. An attempt had been made to gouge out the right eye with a spike ring the day before. There was a cleancut oval incision wound through the upper and lower lids, including the conjunctiva, which separated them from the orbit through most of their extent and caused them to flap outward on a temporal base. The globe was extremely proptosed and could not be replaced. All four rectus muscles were completely severed from their global attachments. The vitreous showed an extensive hemorrhage. Visual acuity was limited to perception of hand movements. The rectus muscles were sought for in the orbit and stitched to their insertions. The lids and conjunctiva were brought back into position. An uneventful recovery occurred. The patient was reexamined

about sixteen months later. The eye was somewhat divergent, with some limitation of adduction, otherwise the ocular movements were good. There was pronounced optic nerve atrophy. Visual acuity was 6/9, and the visual field was concentrically contracted, with a small paracentral scotoma. It is assumed that either there had been stretching and tearing of the optic nerve fibers, with an escape of those serving the central field, or the orbital hemorrhage had compressed the peripheral fibers of the nerve proximal to the level at which the macular fibers leave the periphery of the nerve to course in its central position.

The article is illustrated. W ZENTMAYER

MALIGNANT EXOPHTHALMOS. P. SUNDER-PLASSMANN, *Zentralbl f Chir* 69 88 (Jan 17) 1942

According to Sunder-Plassmann, there are cases of exophthalmic goiter in which the exophthalmos continues to increase after removal of the thyroid. These are cases of malignant exophthalmos. In the mild form of malignant exophthalmos conjunctival excision has been effective, but there are also cases in which the exophthalmos increases to a point of perforation of the eye. The author reports a case in which enucleation of the eyes became necessary. In another case conservative measures proved ineffective. Both eyes had advanced corneal ulcers, and spontaneous perforation seemed imminent. The patient required morphine for control of the pain. The visual capacity was practically nil. As a last resort, it was decided to attempt the operation described by Naffziger in 1933, which that author had successfully employed in 6 cases. Bilateral trepanation was done, and then by the intracranial approach complete decompression of the orbit was effected, as well as decompression of the roof of the nerve canal. As had been observed by Naffziger, the ocular muscles were enormously enlarged, and both optic nerves showed extreme edema. The patient tolerated the operation well. The exophthalmos receded rapidly, and complete closure of the eyes became again possible. The corneal ulcers healed. The patient regained normal visual capacity, and her general condition is excellent.

J A M A (W ZENTMAYER)

### Retina and Optic Nerve

A CASE OF ANGIOID STREAKS OF THE RETINA. T H BUTLER, *Brit J Ophth* 28 220 (May) 1944

The chief interest in the case reported by Butler is that he was able to examine the fundi before there was any ophthalmoscopic evidence of abnormality, and that somewhat rapid changes were

observed subsequently. At the time of the first examination the patient complained of metamorphopsia. Vision in the left eye could not be improved and was about 6/12 mostly. Both fundi appeared normal. In about a fortnight vision had failed in the right eye to 6/36 and in the left eye to 6/24. About six months later vision was further reduced, especially in the right eye, in which it equaled less than 6/60. In the right eye there was a large soft exudate rising from the surface of the retina at the macula, which later became white and harder in appearance. In the left eye the macula was normal. The white masses about the disk were noted about three weeks later. The angioid streaks were characteristic, and there was diffuse "pepper and salt" choroiditis.

A few months later the streaks were less apparent, especially in the left eye. Vision in the right eye was reduced to counting fingers at 1 meter, and in the left eye it was 6/6 with correction. The right field showed a central scotoma about 5 degrees in extent. Butler thinks the case supports Law's conclusions that the streaks are probably caused by folds of the retina with a deposit of pigmentary debris between the rods and cones and the pigment layer.

The article is illustrated.

W ZENTMAYER

### Trachoma

STUDY OF TRACHOMA WITH REPORT OF 318 CASES, 233 TREATED WITH SULFANILAMIDE. C GALLAHER, *J Oklahoma M A* 36 185 (May) 1943

Gallaher submits a statistical analysis of 318 cases of trachoma, most of these patients were treated by him during the last four years. One hundred and eighty-eight of the patients were males and 130 were females, 209 were white, 108 were Indians, and 1 was a Negro. Trachoma is rare among the Negro population. All but 3 of the patients received ambulatory treatment. The adults numbered 134, the children, 184. The author abandoned the use of copper sulfate sticks because of the pain associated with their use. If a treatment is too painful, the patients refuse to return. Silver nitrate was used only in cases in which a complicating gonorrheal infection was present. It was not usually repeated. One or more of the following therapeutic methods were used with all cases: sulfanilamide by mouth, in 199 cases, grattage, in 26 cases, brossage, in 2 cases, zinc sulfate, in 58 cases, copper sulfate solution, in 46 cases, sulfanilamide (1 per cent in isotonic solution of three chlorides), in 40 cases, sulfathiazole, in 3 per cent concentration in ointment, in 9 cases, and vitamin A (25,000 U S P units or more daily), in 4 cases. The results of sulfanilamide therapy were such that the drug must

be included in the treatment of trachoma. No treatment with or without sulfanilamide produces beneficial changes in every case. Well over 90 per cent of patients can be assured of some improvement. Sulfanilamide therapy, in combination with other drugs, affords a method which may be used with reasonable safety without hospitalization and without the necessity of prolonged daily treatment and observation. One or more courses of sulfanilamide therapy alone are apt to produce disappointing results. The specific remedy for trachoma is not yet found. The essential nature of the disease, its cause and its treatment remain a problem to be solved.

J A M A (W ZENTMAYER)

### Tumors

RETRO-ORBITAL ADRENAL REST TUMOR L W HUGHES and A AMBROSE, J A M A 126: 231 (Sept 23) 1944

Hughes and Ambrose removed a tumor, more or less olive shaped, from the orbit of a woman aged 21. The growth was situated behind and slightly above the globe and seemed firmly fixed.

Dr H S Martland reported that the tumor was well encapsulated and appeared to be benign. It was composed chiefly of cells which appeared like hepatic cells or cells from the adrenal cortex, arranged in a manner similar to that of the zona fasciculata of the adrenal cortex, with occasional lumen formation. There were many areas of small round cells. Martland was "inclined to interpret the tumor as a congenital fault somewhat in the nature of an adrenal rest (which has been described in the region of the head) and to regard the collection of small round cells as probably of neurogenic origin."

The article is illustrated.

W ZENTMAYER

REPORT OF A CASE OF PRIMARY CARCINOMA OF LACRIMAL SAC J R WHEELER, Brit J Ophth 28: 233 (April) 1944

A man aged 49 had a tender swelling over the lacrimal sac with a granular mass in the region of the right middle turbinate. A biopsy of this mass revealed no tumor cells. A dacryocystectomy with complete removal of the tumor mass was performed and radium applied. The tumor had arisen from basal cells of the epithelium and histologically had some resemblance to an oat cell carcinoma of the lung. The subepithelial

connective tissue of the turbinate was invaded by tumor cells similar to those of the tumor of the lacrimal sac.

W ZENTMAYER

### Therapeutics

LOCAL CHEMOTHERAPY IN EXPERIMENTAL LESIONS OF THE EYE PRODUCED BY STAPH AUREUS J M ROBSON and G I SCOTT, Lancet 1: 100 (Jan 23) 1943

A highly virulent coagulase-positive strain of *Staphylococcus aureus* was used for infection of the rabbit cornea. A twenty-four hour broth culture in a dilution containing 1,500 organisms per cubic centimeter was injected intracorneally. The lesions produced were similar in the eyes of the same rabbit even after twenty-four hours. At this time, however, great variations were evident in the development of the lesion in different animals. Treatment was applied one hour after injection and consisted of hourly instillations of the chemotherapeutic agent for forty-eight hours, followed by hourly instillations during the day until the lesion was healed.

Sodium penicillin was compared with sodium sulfacetimide in 30 per cent and lower concentrations, solubilized sulfathiazole in 15 per cent solution and tyrothricin in a concentration of 1 milligram per cubic centimeter (tyrothricin consists of 15 per cent gramicidin and 85 per cent tyrocidin). One eye of the experimental animal was treated and the other used as a control. Penicillin was more effective than the other compounds, leaving slight residual scars, whereas in the control eyes lesions classified as moderately severe or severe developed. Sodium sulfacetimide was also definitely beneficial, but less so than penicillin. Ten and 30 per cent solutions of sulfacetimide were equally effective. In 2.5 per cent solution the drug did not exert any definitely beneficial effect. The results of the treatment with solubilized sulfathiazole and with tyrothricin were disappointing. When therapy was initiated twenty-four hours after the infection, no significant benefit was obtained with any type of treatment.

Instillations of penicillin rendered the conjunctiva free of *Staph aureus*, in contrast to the treatment with 10 per cent sodium sulfacetimide, which did not influence the flora noticeably. Early and continued treatment with penicillin or sulfacetimide is required for the best results.

L VON SALLMANN

# Society Transactions

EDITED BY DR W L BENEDICT

## AMERICAN OPHTHALMOLOGICAL SOCIETY

JOHN GREEN, M D, *President*

WALTER ATKINSON, M D, *Secretary*

*Eightieth Annual Meeting, Hot Springs, Va.,  
May 29-31 1944*

### Evaluation of the Visual Acuity Symbols DR WALTER H FINK, Minneapolis

The presentation is a critical survey of the visual acuity symbols which are being used today. These symbols cannot be considered accurate from a scientific standpoint and are comparable to yardsticks of variable length.

A new symbol is presented which fulfils more of the requirements of the perfect symbol as suggested by Landolt.

#### DISCUSSION

DR LE GRAND H HARDY, New York. The author has done a splendid piece of work in making comparative tests, but I do not believe many ophthalmologists will be influenced to change their testing symbols because the test itself is a highly artificial laboratory experiment, which, unless correlated directly with the problems of occupation, experience, duties, etc., may assume an incommensurate importance.

The inaccuracy of the symbol is only one of many factors involved in testing visual acuity. I should not concede that the symbol used is the most important factor in the test.

Dr Fink offers some helpful suggestions aimed at a compromise between "interesting" and "accurate" test symbols, but this problem is far from being solved, as is true also of the problem of avoiding fatigue and reducing the effects of memorization and guessing.

DR S JUDD BEACH, Portland, Maine. One cannot be told too often that charts that are suitable for refraction are unsuited for estimating visual acuity. The alphabet is a notoriously unreliable vision test. Therefore I think the broken ring, with three or multiple breaks, is likely to be useful. Furthermore, the *E* varies in distinctness according to the axis of the cylinder. A patient requiring a high vertical cylinder may recognize an *E* several sizes smaller than when the axis of the cylinder is oblique.

### Removal of the Ruptured Capsule After Operations for Cataract DR F H VERHOEFF, Boston

This paper was published in full in the November 1944 issue of the ARCHIVES, page 407.

#### DISCUSSION

DR JOHN W BURKE, Washington, D C. I want to show a capsule forceps which has been called the Lambert forceps, though that is not its correct name. This pair was made by Tieman and has the advantage of opening vertically, rather than horizontally.

DR ARNOLD KNAPP, New York. I think this topic is a timely one, and, personally, I am glad to hear that some one else has had capsule rupture. I have always maintained, and have proved it to my own satisfaction, that if one uses the traction method of intracapsular extraction until after the subluxation of the lens, and then releases the grasp of the capsule forceps and expresses the cataract by use of the loop and the hook, fewer capsules are ruptured. Ruptures of the capsule occur under three conditions. First, at the start, when the capsule is grasped, particularly when the capsule is thin and tense. The condition is then the same as in an extracapsular cataract extraction. Second, in the middle of the procedure, generally owing to an awkward movement on the part of the operator or of the patient. With the rupture of the capsule there is frequently a rupture of the hyaloid membrane, with prolapse of vitreous. Third, after extraction of the cataract. It has been my experience that it is not difficult to grasp the capsule with the blunt forceps without complications if the illumination is good and, particularly, if one waits a few minutes to allow regeneration of the aqueous. It is of the greatest importance that no capsular tags remain in the incision.

DR F H VERHOEFF, Boston. I am surprised that Dr Knapp brings up the question of the relative frequency of rupture of the capsule with different methods of intracapsular extraction. He has admitted that he succeeds in removing the cataract intact in only 50 per cent of his cases. For my method, this would be a disgraceful record. In reporting several hundred cataract operations he included only those in which the cataract was removed with its capsule. He said nothing as to the results in the equal number of his cases in which the capsule was ruptured during attempted intracapsular extraction. If these



results were not considerably inferior to the others, it would seem that the intracapsular operation should be abandoned. In answer to a question from another discussor I think that fluorescent illumination would aid in the finding of a ruptured capsule, but in the procedure described I have found it unnecessary.

**Complicated Cataract Associated with Spontaneous Detachment of the Retina** DR BERNARD SAMUELS, New York

This paper was published in full in the November 1944 issue of the ARCHIVES, page 416

DISCUSSION

DR ARNOLD KNAPP, New York. Now that all patients with retinal detachment are examined much more carefully, I am sure all have been impressed, as I have, with the frequency of an opacity at the posterior pole of the lens in cases of retinal detachment. I should like to ask Dr Samuels whether this opacity is due to the presence of the vesicular cells which he has demonstrated in his slides.

DR BERNARD SAMUELS, New York. In regard to the nuclear sclerosis, these eyes were mostly those of patients of mature years, so that it was thought the detachment had little, or nothing, to do with the condition of the nucleus.

I am unable to answer the question as to the permeability of the lens capsule.

In answer to Dr Knapp's question, I have no doubt that the liquefaction of the cortical substance and the formation of vesicular cells at the posterior pole may at times account for the opacity seen there clinically.

**Congenital Glaucoma and Bilateral Cataract Treated with Goniotomy and Needling: Report of a Case** DR THOMAS D'ALLEN, Chicago

An infant, seen at the age of 4 months, had low grade, but typical congenital glaucoma (hydrophthalmos), with enlarged, slightly hazy corneas, fairly deep anterior chambers, apparently normal irises and congenital cataracts. The tension of each eye was reduced with repeated goniotomies. When the anterior segments returned to normal, the pupils were dilated, without increase in tension, and the lenses were needled successfully.

DISCUSSION

DR PETER C KRONFELD, Chicago. I am grateful to Dr Allen for the opportunity of examining and following closely his interesting patient, whose left eye undoubtedly was hydrophthalmic. While spontaneous remissions do occur in cases of congenital glaucoma, it seems reasonable to assume that in the eye under discussion the normalization of the intraocular pressure and the clearing of the cornea are to be credited to one or several of the surgical procedures performed by Dr Allen.

As a criterion of the success of his treatment he mentions that atropine could be used freely. There I beg to differ. Atropine has not been shown to cause appreciable increases in intraocular pressure in hydrophthalmic eyes.

The question arises whether the gonioscopic findings permit any statement with regard to which operation caused the normalization of the intraocular pressure. As far as I could see, little embryonic tissue was lying on the trabecula, and no furlow or groove was present in any of its visible portions. The anterior wall of the angle had apparently been incised in several places, but these incisions had healed over or were covered with peripheral anterior synechias. One clearly visible incision lay anterior to the line of Schwalbe. In the lower temporal quadrant a shallow cyclodialysis area seemed to be present. The case might be summed up by saying that the intraocular pressure in a hydrophthalmic eye was normalized probably by a cyclodialysis performed by the devious route through the anterior chamber.

DR EVERETT L GOAR, Houston, Texas. Not every one is equipped to do goniotomies, and some do not believe in them much, perhaps from lack of experience. However, there is an operation which any one who can hold a keratome can do safely—that is, an iridencleisis through a scratch incision, as advocated by Elschning for his "iridectomy ab externa." I have performed this operation on 5 hydrophthalmic eyes and have been able to follow some of the patients for four years or more. They have all done well. It is important to treat such children early, before there is too much infiltration of the cornea or permanent damage to other structures.

DR THOMAS D ALLEN, Chicago. I wish to thank Dr Kronfeld for discussing this paper. I do not quite hold with Dr Barkan that one should always open Schlemm's canal. I have, on several occasions, obtained a definite internal cyclodialysis as a result of the goniotomy, and in one of the eyes reported on in this paper there may be an internal cyclodialysis. Although I perform a cyclodialysis when I believe it necessary, I am a little loath to do it because of the hemorrhage that often follows, a massive hemorrhage in the anterior chamber may be dangerous. Hemorrhage did not occur as a result of any of the operations on this baby. The advantage of this operation is that the cornea becomes smaller and clearer, the tension drops and remains low, the pupils remain central and round and the media are clear, so that a good view of the fundus is easily obtained.

I wish also to thank Dr Goar for his discussion. I have not given up iridotaxis in cases of congenital glaucoma, but I feel that if one can obtain good results without distorting the pupil, an advance in the operative technique has been made.



**Glaucoma Due to Peripheral Anterior Synechias After Operation for Cataract** DR PETER C KRONFELD and DR JOSEPH S HAAS (by invitation), Chicago

This paper was published in full in the March 1945 issue of the ARCHIVES, page 199

DISCUSSION

DR LAWRENCE T POST, St Louis Dr Kronfeld sent me a resume of his paper before this meeting I cannot discuss any phase of the subject of his thesis from other than a theoretic standpoint because I was unable to repeat any of the procedures But for my own satisfaction and as somewhat pertinent to the discussion I reviewed 20 cases of glaucoma following cataract extraction from my own records and those of the eye clinic of Washington University The data in these cases admittedly too few to be more than suggestive, are tabulated to illustrate the relationship of delayed closure of the anterior chamber to other causes of this type of glaucoma I also was interested in a comparison of McLean sutures and conjunctival sutures in preventing delayed closure of the anterior chamber

Probable Cause

Delayed reformation of anterior chamber (1 e, longer than 3 days)	11
Hemorrhage into anterior chamber	3
Unexplained cause	3
Postoperative iridocyclitis	1
Capsule in wound	1
Epithelization of anterior chamber	1

Closure of the anterior chamber was delayed in 3 of 6 cases in which McLean sutures were used or in 50 per cent

Closure was delayed in 8 of 14 cases in which conjunctival sutures only were used, or in 57 per cent

These results suggest that closure by the former method is more effective, but the series is too small to show more than a trend Possibly, also, there were errors of technic in using the McLean sutures

The occurrence of hemorrhage into the anterior chamber in 6 of 20 cases is interesting, as is the fact that 4 of the 20 eyes were from 3 diabetic patients

DR JONAS FRIEDENWALD, Baltimore I should like to add one suggestion to the speculation as to the mechanism concerned in the morning rise of pressure in these cases Dr Kronfeld has shown that the pressure rises during activity Some time ago, Dr Buschke and I showed that the secretory mechanism is under adrenergic control It is possible, therefore, that the secretory activity might be less during sleep than in waking hours, owing to the difference in the activity of the adrenal glands With pentobarbital the activity of the adrenal gland is greatly reduced This as-

sumption might be put to experimental test, and this is my reason for making these comments, by giving the patient an injection of epinephrine sufficient to produce a slight adrenalinemia during the period of the low pressure One would expect that this would produce a rise of pressure On the other hand, ergotamine antagonizes mainly adrenergic actions Parenteral administration of ergotamine might temporarily prevent the rise of pressure in these cases

DR PETER C KRONFELD, Chicago Tentatively, Dr Haas and I have drawn the conclusion from our findings that in the normal human eye the rate of fluid production is greater during waking hours than during sleep Such a physiologic increase in fluid production would explain the morning rises in intraocular pressure observed in our patients We are grateful to Dr Post for his discussion and shall follow the suggestions made by Dr Friedenwald

**Deep Chamber Glaucoma Due to Formation of a Cuticular Product in the Filtration Angle**  
DR ALGERNON B REESE, New York

The endothelium on the posterior surface of the cornea produces a cuticular product (Descemet's membrane) The same endothelium continued into the filtration angle can likewise lay down this cuticular product under provocation When this takes place along the internal surface of the pectinate ligament and in the interstices of the trabeculae, it can produce a deep chamber glaucoma The changes of the endothelium are similar to those seen in cases of dystrophia epithelialis corneae In the presence of the glaucoma, the corneal changes may be confused with bullous keratitis or pannus Cases of deep chamber glaucoma of this type were described and analyzed, and various stages of the pathologic process were illustrated

DISCUSSION

DR PETER C KRONFELD, Chicago The pathologic picture of partial or complete lining of the anterior chamber with a cuticular membrane is a fairly common finding in eyes with glaucoma following trauma, endogenous uveitis or retinal detachment I had always considered these membranes as late pathologic changes, not related to the original pressure-elevating mechanism Dr Reese now presents the thesis that obstruction of the corneoscleral trabecula by the deposition of hyaloid material on its inner surface and in its interspaces is the direct cause of certain glaucomas To me it seems that Dr Reese has come as close to having proved his thesis as it is possible at this time His material consisted of eyes that were removed because of intractable pain, which was most likely caused by recurrent corneal bullae or ulcers It is to be hoped that the missing link in his chain of evidence will be provided when an early state of this type of glaucoma becomes

available for pathologic examination through the accidental or coincidental death of its bearer. Until then, one might look for traces of these cuticular membranes on the pieces of iris excised during trephine operations. Goniocopy cannot be expected to throw any light on the subject.

From the study of Dr. Reese's paper it appears highly probable that he is describing a group of glaucomas characterized not only by similar pathologic changes but by a similar clinical course. In all but 2 of his cases corneal changes were in the foreground at an early stage of the glaucoma. Dr. Reese could have brought out this point more strongly had he mentioned the amount of vision present at the time of enucleation. If at that time the projection of light was still good in most of his cases, the glaucomatous process could not have been far advanced. To me it seems probable that Dr. Reese has described here a definite pathogenic entity among the glaucomas.

Dr. Reese attributes the failure of trephine operations in 4 of his cases to the growth of endothelium into the trephine opening and to the laying down of a cuticular product which partially fills the trephine opening and prevents filtration. Here I beg to differ. The openings made in successful trephine operations become lined with endothelium, which may lay down hyaloid material to a greater or lesser extent. I doubt that a complete cuticular lining of a trephine hole could by itself close off the opening, with the intraocular pressure acting on it. I believe it takes tissues with greater strength and resistance to oppose and block the filtration of intraocular fluid through a trephine hole.

DR. F. H. VERHOEFF, Boston. Dr. Reese's interpretation of his cases is so satisfying that I hope it will not be disproved. However, thirty-two years ago, I reported a few cases that may seem to throw some doubt on it, and since then I have seen many similar cases. I brought forward evidence I still believe to be valid, that sclerosis of the pectinate ligament sometimes results from a peripheral anterior synechia that later becomes freed. The evidence consisted chiefly in the fact that in places I found the iris still in the act of pulling away from the ligament. In some sections of one of the 10 eyes described, I found the exact condition now described by Dr. Reese, but, on making sections in other quadrants of this eye, I found places where the ligament was coated with connective tissue instead of elastic membrane, and other places where part of the ligament was covered with elastic membrane and the remainder with adherent iris. More important still, I found that nowhere did elastic membrane extend between the adherent iris and the ligament. On the contrary it extended around the false angle for a short distance over the free surface of the iris. It was evident, therefore, that here the new membrane had been formed after the occurrence of a peripheral anterior synechia, and hence was probably a result, not the cause, of the glaucoma.

### Errors in Diagnosis in Cases of Intraocular Tumor (Suspected or Real). DR. WILLIAM EVANS BRUNER, Cleveland

Lessons from failures in diagnosis, either the errors of my colleagues and myself or those of others, may be obtained from the following cases.

CASE 1—A man aged 58 had a condition previously diagnosed as detachment of the retina. Our diagnosis was intraocular tumor. On enucleation a spindle cell sarcoma was found.

CASE 2—A man aged 55 had a condition diagnosed as probable serous detachment of the retina. Operation by his own oculist resulted in temporary improvement. Redetachment and, later, glaucoma necessitated enucleation, with the finding of melanotic sarcoma.

CASE 3—A woman aged 42 had been previously treated for carcinoma of the cervix. She had a retinal detachment with shadow. The diagnosis was probable carcinoma. She was sent back to the original clinic. The oculist thought the condition was serous detachment and operated for this. The subsequent history is not known.

CASE 4—A woman aged 55 had retinal detachment with shadow, there was no tear or hole. The diagnosis was probable intraocular tumor. An oculist in another city pronounced the condition serous detachment and performed operation. Four years later there was no evidence of tumor.

CASE 5—A man aged 27 had a condition which we diagnosed as intraocular tumor. Operations by other oculists were performed. The sclera was punctured, and, later, trephination done. Four years later enucleation revealed a tumor.

CASE 6—A girl aged 18 years had detachment with shadow and increased tension. She gave a history of a fall. Our diagnosis was probable subretinal hemorrhage, and she was treated for this condition. Another oculist made the diagnosis of tumor and removed the eye. The pathologic report was subretinal blood clot with glaucoma. There was no tumor.

### DISCUSSION

DR. A. D. RUEDEMANN, Cleveland. The excellent, thought-producing report of Dr. Bruner makes all realize that the diagnosis of intraocular tumor is not always difficult, but that the underlying causes require skill and study to determine. More than one visit to the office may be needed before a definite conclusion can be reached, or a stay in the hospital, with retrobulbar transillumination, may be required.

DR. F. H. VERHOEFF, Boston. Theoretically, there should be cases of intraocular tumor in which the separated retina shows a hole or is definitely tremulous, but I have never seen one. Has Dr. Bruner ever seen a hole in the retina in a case of intraocular tumor?

DR. WILLIAM EVANS BRUNER, Cleveland. I wish to thank those who discussed my paper.

I was interested to hear Dr Verhoeff say that he had never seen a case of intraocular tumor with a hole or tear in the retina. This has also been my own experience, but, as previously stated, I do not understand why it should be so.

### **Bilateral Metastatic Carcinoma of the Choroid, with Roentgen Ray Therapy of One Eye** DR FREDERICK C CORDES, San Francisco

A case of bilateral metastatic carcinoma of the choroid secondary to a tumor of the breast in a woman aged 31 years was reported. One eye was enucleated, and the diagnosis of metastatic carcinoma was confirmed by microscopic examination. With the appearance of a similar growth in the second eye, roentgen irradiation was employed. This was followed by disappearance of the tumor and retention of 20/20 vision in the eye.

Fourteen months later there was a recurrence, and the tumor again responded to irradiation. With this method it was possible for the patient to retain 20/20 vision up to the time of her death (twenty-three months after enucleation).

While the ultimate prognosis is hopeless, the possibility of retaining useful vision by means of palliative treatment should receive consideration in cases of metastatic carcinoma of the choroid.

#### DISCUSSION

DR A N LEMOINE, Kansas City Mo. I should like to report further on the case of bilateral carcinoma of the choroid which I reported in 1943 in the discussion of Dr Ellett's paper at the meeting of the American Ophthalmological Society (Metastasis of Malignant Tumors to the Eye. Report of Two Cases, ARCH OPHTH 32:145 [Aug] 1944). The patient died just a year after roentgen ray therapy of both eyes was instituted.

At the time the therapy was begun the patient had 10/200 vision in the right eye and 20/200 in the left eye, and the treatments produced complete recession of the growth in the left eye, with great reduction in the size of the lesion in the right eye. In October vision was 20/100 in the right eye and 20/30 + in the left eye, she retained useful reading vision in the left eye until the time of her death.

I strongly recommend the treatment as a therapeutic measure that will greatly add to the happiness of the last days of these unfortunate patients.

### **Spontaneous Retinal Reattachment** DR ARNOLD KNAPP, New York

This paper was published in full in the November issue of the ARCHIVES, page 403.

#### DISCUSSION

DR H S GRADLE, Chicago. Is it not probable that Dr Knapp has failed to differentiate between spontaneous reattachment of the retina and self-limited detachment? The two conditions are dif-

ferent. Spontaneous reattachment occurs in a small number of cases and leaves no aftermath except for the occasional presence of white retinal striae. On the other hand, self-limited detachment corresponds to the photographs shown by Dr Knapp and has the following characteristics: (1) a pigmented line of demarcation, (2) detachment of the retina peripheral to this line of demarcation, persisting for many years, (3) preservation of vision according to whether or not the macula is involved, and (4) history of trauma.

Histologically, it has been shown that the white retinal striae lie within the retina proper and represent the organization of coagulated fibrin (*Fibringerinnseln*). The lines of demarcation, however, represent an organized exudation between the retina and the choroid and are always pigmented.

DR ARNOLD KNAPP, New York. I did not read all of my paper, in it is a full description, with references from the literature which cover many of the things that Dr Gradle was good enough to point out. I did not get the impression that these white wavy lines were in the retina. According to the histologic examinations which have been made, they were organized changes in the sub-retinal tissue. Shallow detachments do not occur in many cases, but sometimes there is a limited area of detachment directly around the hole. I think the presence of the limiting boundary has not been sufficiently noted, and when that is present it can be taken for granted that the detaching process has stopped.

### **Red-Free and Binocular Ophthalmoscopy** DR RALPH I LLOYD, Brooklyn

The results of using these instruments in examinations of the fundus over a number of years were summarized. Each makes a limited but valuable contribution to diagnosis of certain diseases of the fundus.

#### DISCUSSION

DR JONAS FRIEDENWALD, Baltimore. Dr Lloyd has restated part of the arguments of Vogt and Gullstrand, which constitute one of the classics in the literature of ophthalmoscopy. The work of these two great founders of modern ophthalmoscopy has never been adequately reviewed, and I shall not attempt to do so in the brief time allotted for the discussion of Dr Lloyd's paper.

Vogt's choice of the red-free light filter arose from his effort to make visible in vivo the yellow color of the macula seen post mortem. With this light a yellow tinge is readily visible in the macular region, but Gullstrand demed, with many arguments, that this indicates the presence in vivo of a yellow pigment. The argument as to the existence of this yellow pigment was, however, soon refuted by the accidental discovery that more detail was visible in the eyeground illum-

nated with red-free than with white light. Vogt attributed this increased detail to increased contrast in the ophthalmoscopic picture. It can easily be shown, however, that, in addition to the increased contrast, there is an increased resolving power in the optical system, i.e., finer details are visible. The source of this increased resolving power was found to be the decrease in the chromatic aberration of the optical system which occurs when part of the spectrum is eliminated from the illuminating system. Since this is true, it is possible to increase the resolving power still further by using light that is more nearly monochromatic. Just what portion of the spectrum should be chosen for the monochromatic illumination depends on what one is looking for.

DR F. H. VERHOEFF, Boston. More than forty years ago I discovered that when after fixation in a solution of formaldehyde the macula was yellow in an enucleated eye, the sections showed ganglion cells in the macula and that when the macula was not yellow sections showed no ganglion cells there. I concluded, therefore, that the yellow color resided in the ganglion cells and was probably due to their lipid content. Ever since then I have given this explanation to my students. I have never searched the literature to ascertain whether any one before or since has given this explanation or proved it to be incorrect. Perhaps Dr. Lloyd, from his extensive study of the literature, can enlighten us on this matter.

DR RALPH I. LLOYD, Brooklyn. I have nothing whatever on which to base an opinion as to the location of the pigment seen in the normal retina immediately after removal from the eye.

#### Analysis of Cases of Aniseikonia DR BEULAH CUSHMAN, Chicago

This paper was published in full in the January 1945 issue of the ARCHIVES, page 9.

#### DISCUSSION

DR L. T. POST, St. Louis. My associates and I have been making these tests at Washington University, in St. Louis, for ten years. It seems obvious that whereas aniseikonia is present in a great many people it causes symptoms in a relatively small number. The question whether one can say that the patient is relieved by aniseikonic correction or not is not entirely simple. I reported, 100 cases four or five years ago, drawn at random from the files of patients who had worn their correction over nine months, 79 per cent had been improved, and 49 per cent, completely relieved. We have had about 1,200 patients for whom eikonic corrections have been ordered. Of these, I have examined about 450. From the records of 100 of these patients I found that 75 were given no change in their fundamental glasses of as much as 0.5 D in the spherical or astigmatic correction. I did not, however, take into account small changes of axis. Of the remaining 25, 22

had a change between 0.5 and 1 D, 3 had more than 1 D. We thought it wise to make such changes as we found. My patients have three checks by my associate, by myself and by the aniseikonia technician. In many cases young persons return for a check with a cycloplegic, and we combine the results of all the refractions and incorporate them in the eikonic correction. I do not think these refractive changes are going to prove an important element in the end result. The question, I think, is whether the patients who are helped are the ones who get even a small change in refraction. Most of our patients do not seem to have a great deal of muscular trouble, but there are certainly a few who do. When anything obvious has been found, such as a bad muscle imbalance, we have not usually given the eikonic correction but have sent them back to the physician who referred them.

DR LEGRAND H. HARDY, New York. I should like to mention two rather widespread misconceptions.

The first is that all, or most, aniseikonic patients are neurotic. While in many cases this is true, it most certainly is not true in all cases. Many physicians are likely to send neurotic patients to the aniseikonia clinic as a last resort or in the hope of being freed from them. This contributes considerably to the difficulties of formulating an accurate evaluation of aniseikonia and its clinical correction. The fact that a patient, having worn aniseikonic lenses for a period of from two months to two years, finds no further need for wearing them, in spite of the continuance of a demonstrable aniseikonia, does not prove that the condition was neurotic. The fact that among symptom-free subjects definite, and sometimes high, degrees of aniseikonia are found indicates the presence of a compensating mechanism. Such compensation, I believe, can be trained, and tolerances to size differences can be acquired and amplified.

The second misconception is that orthoptics is concerned with muscle imbalances (chiefly strabismus), and muscle imbalances only. This is not true.

I have rather imperfectly described orthoptic training as a method designed to develop or restore the normal, integrated binocular functions by means of graded exercises and training. It might possibly better be described as a series of methods used in the acquisition of ocular skills. Speed of fusion, speed of recognition, speed of adjustment and stereopsis, among other skills are all subject to improvement through training. According to the more generalized view, aniseikonia will probably fall within the ambit of orthoptics. Our technician at the Eye Institute has frequently encountered great difficulties in measuring the aniseikonia particularly for near

vision, in subjects who have developed a high amplitude of fusion. The fusion training has greatly modified the aniseikonic picture.

**Johannes Muller. A Sketch of His Life and Ophthalmologic Works** DR BURTON CHANCE, Philadelphia

This paper was published in full in the November 1944 issue of the ARCHIVES, page 395

#### DISCUSSION

DR F H VERHOEFF, Boston. I should like to ask Dr Chance whether he could say something about the circle of Muller? I should like to know what Muller called it, what importance he gave to it and who first attached his name to it. No doubt if he had attempted to define aniseikonia, he would have done so in terms of corresponding points. The Dartmouth group do not mention corresponding points when they attempt to define this condition.

**Visual Symptoms Caused by Digitalis** DR FRANK D CARROLL, New York

Digitalis in normal dosage may produce visual symptoms with little or no other evidence of drug intoxication. Four cases seen by the author were reported. Two of the patients stated that everything appeared covered with snow, one, that she saw shiny objects "like goldfish," and the fourth complained of bright floating spots in her visual fields. All these symptoms disappeared within five days when the drug was stopped.

#### DISCUSSION

DR T H JOHNSON, New York. The hallucinations in Dr Carroll's cases could have been caused by a toxic effect of the digitalis on the retina or on the higher visual centers. There are two areas in the occipital cortex which respond to stimuli, the visiosensory and the visipsychic centers. Stimulation of the visiosensory area may produce hallucinations which consist of flashes of light, luminosities or spectral appearances, while stimulation of the visipsychic area recalls stored memory pictures and reproduces panoramas, pictured scenes and scenes of action. The theory generally accepted is that crude visual hallucinations are the response to stimulation of the conduction tracts or higher centers in the occipital lobe, while complex phenomena are the result of the stimulation of the afferent visual pathways. However, it is well known that local lesions in the retina produce crude hallucinations. All ophthalmologists have had cases in which local changes in the retina have produced flashes of light and luminous scintillations, and there are many reports in the literature of crude hallucinations which were caused by local retinal lesions. The temporary loss of vision may be explained by the fact that the retinal arteries may have become spastic under the influence of the drug, causing temporary loss of vision, such as is often

associated with arteriolar spasm in arterial hypertension. It would be hard to differentiate between obscuration of vision caused by spasm of the retinal arterioles and that caused by spasm of the arteries in the occipital lobe.

DR FRANK D CARROLL, New York. I want to thank Dr Johnson for his comment. All can profit by rereading his thesis on visual hallucinations presented before this society some years ago (*Tr Am Ophth Soc* 31: 344, 1933). It still remains one of the outstanding works on this topic. As to his suggestion regarding the possibility that the visual symptoms due to digitalis may be associated with vasospasm of the retinal vessels, I have not observed any such change and think that in all probability there is a direct toxic action on the cells of the central nervous system.

DR D F Gillette, of Syracuse, has, I think, made an important contribution on this subject. He has just sent me the report of 2 cases of retrobulbar neuritis due to digitalis. Both patients had central scotomas and marked reduction of vision. Both recovered promptly when use of the drug was stopped. One had a temporary recurrence when again placed under medication with digitalis. This quickly disappeared after the drug was stopped. So far as I know, these are the first definite cases of retrobulbar neuritis due to digitalis clearly described, and I hope Dr Johnson will report them in detail.

**Albinism with Coexisting Anomalies of the Central Nervous System** DR C P CLARK, Indianapolis

A brief discussion of albinism was given. A few case histories were reviewed, and anomalies accompanying albinism, particularly of the central nervous system, were noted.

#### DISCUSSION

DR HARRY S GRADLE, Chicago. This excellent paper by Dr Clark presents so many opportunities for discussion of various phases that I wish to limit myself to one particular aspect, namely, the histologic picture.

The first description of albinism was made by Fritsch in 1907, but it was not until 1913 that Elschnig presented serial sections of an albinotic eye. I wish to quote from his article (*Arch f Ophth* 84: 401, 1913). "Serial sections showed the absence of a fovea centralis. In this central area of the albinotic eye the ganglion cell layer was somewhat thickened, as in the normal eye, and the nerve fiber layer was reduced to a layer of very delicate nerve fibers, which could be differentiated sharply from the membrana limitans interna, in an area of about 6 mm diameter. In the center of this area, the rods and cones were somewhat elongated, and the external nuclear layer was somewhat thinned and merged indistinctly with the 'sponged-over' inner nuclear layer. The other layers were about normal."



These findings were later corroborated by Gilbert, Velhagen and Usher

Such lack of foveal differentiation can easily be detected ophthalmoscopically in cases in which the nystagmus can be controlled. There are to be seen only a slight depression of the fovea and a marked diminution in the foveal reflex

Anatomically, this picture is much the same as that shown in the embryonic eye between the sixth and the seventh month, according to Bach and Seefelder. The correlation of the ophthalmoscopic and the histologic picture explains the poor vision in these cases

May I add a point found in practical experience? When such albinotic children are fitted between the ages of 8 and 12 years, they are able to use telescopic spectacles so satisfactorily that their collegiate education can be completed without great difficulty

#### Amyloid Disease of the Conjunctiva Dr NORMA B ELLES, Houston, Texas

A discussion of primary and secondary amyloid disease of the conjunctiva was given, with presentation of a case of the primary type which had been under observation for three years

The nature of amyloid and the process of its formation in the tissues are still debatable. Various more recent experimental investigations on amyloid, from both the pathologic and the biochemical viewpoints, were reviewed

Amyloid disease is to be differentiated from hyaline degeneration and plasmoma

#### DISCUSSION

DR ALGERNON B REESE, New York. Dr Elles has presented the most thoroughly studied case of amyloid disease of the eye that I have encountered on record. She has made a particular effort to rule out a virus infection as a factor. In her paper, she gives a complete discussion of the literature and the theories advanced. She champions the theory that the disease is a disturbance of protein metabolism whereby the rate of formation of catabolic protein products exceeds the ability of the tissue to dispose of them. She believes that there should be surgical removal of redundant areas which are disfiguring or which jeopardize the cornea. The disease in her case showed slow regression with the administration of fresh liver and preparations of vitamins A and C

#### Diabetic Iridopathy Dr C A CLAPP, Baltimore

There frequently occur in the course of diabetes mellitus cellular changes in the iris, especially in the pigmented epithelium, which are not inflammatory. These changes should be termed

iridopathy instead of iritis, just as noninflammatory retinal lesions are termed retinopathy instead of retinitis

#### DISCUSSION

DR W P BEETHAM, Boston. Changes in the iris attributed to diabetes can be grouped as follows

In the first group are the changes of inflammatory nature. In my opinion, this group deserves no further comment. Iritis and uveitis present the same frequency, etiologic factors, course and prognosis, irrespective of whether diabetes exists or not

The second group consists of pupillary abnormalities. This, likewise, is of minor interest at present

The third group consists of changes characterized by capillary proliferation. A vascular membrane is not uncommonly seen on the iris with various pathologic conditions. When the vessels are of sufficient size to be recognized grossly, "rubeosis iridis" exists. This vascularization occurs often with hemorrhagic glaucoma, hemorrhagic glaucoma occurs not infrequently with diabetes, hence the term "rubeosis iridis diabetica". In all of these eyes glaucoma either is present or soon develops. All eyes exhibiting such vascular changes on the iris present similar vascular changes in the retina, "diabetic retinopathy"

The fourth group represents changes in the retinal pigment epithelium. One of the commonest of lesions, as Dr Clapp has pointed out, is the edema and cystic degeneration of the retinal pigment layer. With the necrosis of the pigment epithelium, small vesicles form which contain pigment granules, fragmented nuclei and glycogen

Dr Clapp's suggestion of using the term "iridopathy," as meaning changes in the iris of noninflammatory character, is most agreeable. I wonder, however, whether the term should include both glycogen infiltration and vascularization of the iris. The similar term retinopathy refers chiefly to vascular proliferation in the retina, and it would seem that the term iridopathy should refer to similar changes in the iris. The word, therefore, would have little meaning if limited to this use. If, on the contrary, it is used to designate cystic degeneration and glycogen infiltration, it refers to a condition dissimilar to that indicated by the corresponding term retinopathy. If it is used to designate these changes, the term will not be used clinically, as the actual diagnosis of these alterations must really be made pathologically

DR A B REESE, New York. Has Dr Clapp any explanation of the fact that these changes occur only in the pigment epithelium of the iris, and not in the pigment epithelium elsewhere?

DR C A CLAPP, Baltimore. In the first place, I feel that the term iridopathy should not be



limited to diabetic conditions alone. I tried to limit this report to this one phase of the disease of the iris, but I believe that similar changes may occur in other diseases, as well as in diabetes.

### Angioid Streaks in the Deep Layers of the Retina DR ARTHUR J BEDELL, Albany, N Y

Stereoscopic examinations confirmed by photographs prove that these curious, frayed-edged streaks are anterior to areas of choroidal destruction and posterior to the retinal vessels. The progressive changes in the fundus which had gradually taken place during several years of observation were recorded. A study of them gave the warranted impression that the streaks found in conjunction with choroiditis, senile macular degeneration and papilledema are probably not the result of a common cause but represent the coincidence of the combination of separate diseases. Broad and extensive streaks have been seen in fundi that were otherwise normal.

#### DISCUSSION

DR GRADY E CLAY, Atlanta, Ga. In 1932, I was the first to publish in this country a report on the association of angioid streaks and pseudoxanthoma elasticum (*ARCH OPHTH* 8 334 [Sept.] 1932), since that time the reported association has become too frequent to be coincidental, and therefore the pathologic picture must be described. Since the original report, I have seen 63 more cases, in 30 per cent of these cases the streaks were associated with pseudoxanthoma elasticum, and in 15 per cent they were familial. I have found no other related disease in this group. Nineteen patients in my series were hospitalized, and a careful study of this group revealed no other associated disease. One patient with only a few streaks died recently of hypertensive disease. An autopsy was performed, and one eye was obtained. The complete report is not yet ready for publication.

I still believe that the disease is one of the blood vessels associated with degeneration of elastic tissue and that the earliest changes seen are hemorrhages and the formation of the streaks in the choroid. After this acute period has passed, which may be a year or two, hemorrhages are rarely seen, and no more streaks develop, from this time on there is a slowly developing choroidal atrophy in the areas of the streaks and in these areas the streaks will entirely disappear. Why should there develop such a definite area of choroidal atrophy if this disease is not primarily a disease in the choroid and a disease of the blood vessels?

In my opinion the true pathologic picture is not yet known, and unless one is fortunate in securing an eye early in the course of the disease it will not be known for secondary changes too greatly alter the pathologic picture.

### Toxoplasmosis: Report of Ocular Findings in Twins DR PARKER HEATH, Detroit

This paper was published in full in the March 1945 issue of the *ARCHIVES*, page 184.

#### DISCUSSION

DR WENDELL H HUGHES, Hempstead, N Y. Does not this condition have an acute stage? There must be one, but I have not seen it described.

DR ALAN C WOODS, Baltimore. I should like to ask Dr Heath whether he is interested in toxoplasmosis as a possible cause of choroiditis and whether he has had any experience in regard to such a relation.

### Penicillin Therapy in Ophthalmology DR JOHN H DUNNINGTON and DR LUDWIG VON SALLMANN (by invitation), New York

This paper was published in full in the November 1944 issue of the *ARCHIVES*, page 353.

#### DISCUSSION

DR E V L BROWN, Chicago. This paper, even with its small series of clinical cases, is especially welcome at this time because penicillin has so recently been made available to civilians that few have had opportunity to use it. I have had no such opportunity and must content myself with asking a single question—In view of the relatively small harm which the authors have found that penicillin produces when injected into the rabbit's vitreous and its favorable effect when injected within six to twelve hours after experimental infection of the vitreous, would it now be in order to inject penicillin (early) in cases of severe penetrating wounds of the eye when, say, the lens has been injured and the vitreous body supposedly opened to infection?

DR F H VERHOEFF, Boston. I should like to ask the essayists whether they have investigated the action on retinal function when penicillin in effective concentration was injected into the vitreous. I recall one infected human eye in which injection of a different germicide into the vitreous overcame the infection without producing obvious damage, yet completely blinded the eye.

DR ALAN C WOODS, Baltimore. The use of penicillin is new, and every one's experience is limited. For some time a crude penicillin has been available which has been used with rather conspicuous success in corneal baths or by instillation in cases of staphylococcal conjunctivitis. The purified penicillin has been used by iontophoresis in 8 or 10 cases of staphylococcal corneal ulcers. The results have been distinctly encouraging. It has been used in 2 or 3 cases of purulent panophthalmitis, by direct injection into the eye. In 1 case a trephination had been done on an eye before the man was admitted with

panophthalmitis. There was no improvement with the sulfonamide drugs. He was then given an injection of penicillin directly into the eye, but it had no effect on the disease, and the eye was lost. In another case intraocular injections had no effect. The results of intraocular injections are limited and not outstanding.

DR LUDWIG VON SALLMANN, New York. With reference to Dr Brown's question, a single injection of a small amount of highly purified penicillin may be regarded as a reasonably safe therapeutic procedure considering the unfavorable prognosis of ectogenous infections of the vitreous. This type of injection was applied in 1 case in which clinical signs of panophthalmitis existed, the acute inflammatory signs regressed, but it is too early to judge whether some vision will be restored.

#### Combined Intracranial and Orbital Operation for Retinoblastoma

DR CHARLES E G SHANNON, Philadelphia

A case of bilateral retinoblastoma was reported in which the combined intracranial and orbital operation as suggested by Jean, in 1924, was carried out with apparent success on both eyes. Merits of this operation are discussed.

#### DISCUSSION

DR ALGERNON B REESE, New York. In 1931 (ARCH OPHTH 5: 269 [Feb] 1931) I published the results of the microscopic examination of 119 eyes enucleated with the diagnosis of retinoblastoma. In 43 per cent of the eyes the operative section through the optic nerve was not beyond the extension of the tumor, and therefore residual tumor had apparently been left in that portion of the optic nerve which remained in the orbit. For some time I have felt that these figures are not consistent with those for current cases. Therefore, a similar study was made of 65 eyes enucleated during the past eight years at the Institute of Ophthalmology or at the Memorial Hospital for the Treatment of Cancer and Allied Diseases. Of this group, the tumor had extended into the optic nerve beyond the lamina cribrosa in only 15 eyes, or 23 per cent. The tumor had extended beyond the site where the nerve was severed at operation in only 4 eyes, or 6 per cent. The tumor had extended through the sclera in 7 eyes, or 11 per cent.

The eyes in the older group were enucleated in the period between 1878 and 1929 (fifty-one years), while the eyes in the recent group were enucleated in the period between 1934 and 1942 (eight years). The discrepancy in the figures for these two series seems to be due to the fact that in the older group a diagnosis was not made as early and the optic nerve stump left attached to the sclera was not as long as in the more recent

group. The increasingly lower mortality figures in the past seventy-five years also bespeak earlier diagnosis and the leaving of a longer optic nerve stump at the time of enucleation.

If the optic nerve is severed properly at the time of operation, there is little chance that residual tumor will be left in that portion of the nerve remaining in the orbit. The firm tissue of the optic nerve offers resistance to tumor invasion, and seldom does a tumor extend into the nerve for more than a few millimeters, and practically never as much as 8 to 10 mm.

#### Pathogenesis of Intermittent Exophthalmos.

DR FRANK B WALSH and DR WALTER E DANDY (by invitation), Baltimore

This paper was published in full in the July 1944 issue of the ARCHIVES, page 1.

#### DISCUSSION

DR W L BENEDICT, Rochester, Minn. Intermittent exophthalmos is a rare clinical phenomenon due to venous aneurysm within the orbit and occurs probably only in cases of congenital vascular anomalies. It is to be distinguished from pulsating exophthalmos, which usually is the result of trauma, and the authors have defined the terms with this in mind.

Three cases of intermittent exophthalmos have been seen at the Mayo Clinic, and in only 1 of them was operation performed.

DR FRANK B WALSH, Baltimore. I wish to thank Dr Benedict for his interesting comments. It is gratifying that he seems to be in agreement regarding the production of intermittent exophthalmos by developmental vascular abnormalities.

As regards surgical intervention when indicated in such cases, Dr Benedict seems in agreement with respect to the transcranial approach.

#### Recurrent Erosion of the Cornea

DR PAUL A CHANDLER, Boston

Various types of recurrent erosion of the cornea were described, the literature was reviewed, possible etiologic factors were discussed, and various forms of treatment were evaluated.

#### DISCUSSION

DR RALPH I LLÖYD, Brooklyn. I venture to suggest that in most of the cases reported the erosion was postherpetic. I have a number of similar cases under observation in which there have been recurrences over a period of twelve to fifteen years.

The best treatment is prevention of recurrence by using the moist chamber spectacles or the expansion shield, which can be applied and removed from the spectacles easily.

The herpetic patient carries the virus in the conjunctival sac, and slight trauma allows it to

enter the epithelial layer. Such a patient does not recover full sensation of the cornea, and when the sensation diminishes, there are lowered vitality and recurrence or reinfection.

In some cases of keratitis sicca, lattice dystrophy and Fuchs's dystrophy, the lesions are similar, but the differential diagnosis should not be difficult.

DR PAUL A. CHANDLER, Boston. The neuropathic theory is difficult either to prove or to disprove. My reason for feeling that a damaged endothelium may be a factor is the close analogy between recurrent erosion and vesicular or bullous keratitis, which is evidently due to a defective endothelium.

In regard to changes in sensitivity which Dr Lloyd mentioned. Some of these corneas are hypersensitive, some are normal and some are insensitive, and it is hard to draw any conclusion. It depends on how long the trouble has been present and how severe the bullous keratitis is. In the early stages the pain may be severe, but later the nerve endings are destroyed and there is less pain. Recurrent attacks of herpes are common, but I believe this condition is a different disease than ordinary recurrent erosion of the cornea. In regard to Dr Lloyd's suggestion of wearing protective spectacles to conserve moisture, according to my experience this is the wrong thing to do. As I mentioned before, if one prevents evaporation of tears and thus lowers their osmotic tension, there is more likely to be trouble, as witnessed by the occurrence of attacks after sleep and after weeping. Dr Post's case in which relief was obtained with use of a thermophore treatment illustrates another simple method of treating the disorder. Patients with the microform of this disease usually will not submit to radical treatment, and if given 10 per cent boric ointment to use in the eye at night and instructed to observe care in opening the eyes in the morning, they will get on with a minimum of trouble.

**Mitotic and Wound-Healing Activities of the Corneal Epithelium.** DR JONAS S. FRIEDENWALD and DR WILHELM BUSCHKE (by invitation), Baltimore.

This paper was published in full in the November 1944 issue of the ARCHIVES, page 410.

#### DISCUSSION

DR F. H. VERHOEFF, Boston. This painstaking and laborious investigation is of great scientific interest and importance. The essayists have not attempted to apply their results to clinical problems, but no doubt will do so later. They confirmed and utilized the remarkable fact that colchicine can stop mitosis in the metaphase without otherwise interfering with cell division or

checking the entrance of cells into it. They found no drug whose effect was similar. It would seem, however, that the effect of cold was somewhat similar, since they state that it froze the cells in metaphase without abolishing the other phases of mitosis. A notable discovery was that cervical ganglionectomy reduced the number of cells entering into mitosis and slowed the mitotic cycle. No explanation of these effects was attempted.

The essayists found that localized damage to the corneal epithelium inhibited mitosis in the surrounding cells. They also found that exposure of the corneal epithelium to ultraviolet light notably inhibited mitosis in the exposed area.

The essayists found nothing that stimulated mitosis. Apparently they did not try the effect of heat. *I found that heat generated by radiant energy stimulated mitosis in the corneal corpuscles and in the capsular epithelium.* In one experiment I focused sunlight on the highly pigmented iris of a rabbit. This caused necrosis of the iris in the exposed area and produced in the capsular epithelium behind this area the most abundant and beautiful mitoses I have ever seen—almost every cell was in some stage of mitosis. The capsular epithelium is particularly well suited for such experimentation because it consists of but a single layer and the lens is free from nerves and blood vessels. Among the agents tested by the essayists, I note the absence of scarlet red (sudan IV), commonly believed to be a stimulant to epithelial repair.

The essayists state, in confirmation of other investigators, that epithelial defects in the cornea, even large ones, are repaired by cell migration without multiplication. I should like to ask whether they excluded the possibility that amitotic cell division played a part in the healing process. I found that it occurred in capsular epithelium injured by ultraviolet light. I should also like to ask whether the essayists determined when mitosis began in a repaired area.

The essayists state that even severe exposure to ultraviolet light does not inhibit wound healing. I take it that they found that an exposure which markedly inhibited mitosis did not interfere with the healing of small traumatic defects in the exposed area. This is certainly a remarkable fact. Still more remarkable is their finding that repair can be made by epithelium so severely exposed that it later sloughs off. Their statement that after an exposure which causes sloughing of the epithelium repair promptly begins at the margin of the slough is perhaps of doubtful significance, since the cells making the repair may have received slight, if any, exposure.

DR JONAS S. FRIEDENWALD, Baltimore. Dr Verhoeff's question as to the possible presence of amitotic division is one which we are unable to answer. We have seen no cells in our preparations

with double nuclei, but our failure to find such cells does not rule out the possibility of amitotic division. Current trends of thought among biologists have raised doubts as to the existence of amitotic division as a general phenomenon. In many of the instances in which this type of division was formerly thought to have taken place only mitotic division has been exhibited. In regard to the cornea, the question is still open.

#### **Retrolental Fibroplasia in Premature Infants.**

**V Further Studies on Fibroplastic Overgrowth of the Persistent Tunica Vasculosa Lentis** DR T L TERRY, Boston

This paper was published in full in the January 1945 issue of the ARCHIVES, page 203

#### **DISCUSSION**

DR E V L BROWN, Chicago I have operated in 1 case—on each eye, as advised by Dr Terry. It is too early to determine the results. I am extremely interested in the subject because for years back my associates and I have been taking out such eyes, fearing glioma. After seeing the patient, Drs Bothman, Kronfeld, Kraus, Stough, Fralick and I would each write down separately what we thought the diagnosis should be. I do not know who was wrong most of the time, but I think we were all wrong many times. We have mistaken retrolental fibroplasia for glioma in many cases. In 4 or 6 enucleated eyes seen between 1935 and 1940 there was really retrolental fibroplasia.

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## **News and Notes**

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#### **GENERAL NEWS**

**Postgraduate Course in Ophthalmology, Washington School of Medicine**—The Department of Ophthalmology, Washington University School of Medicine, will resume its eight month postgraduate course on Oct 1, 1945. The course will be limited in number. For further details, address Dr Lawrence T Post, 640 South Kingshighway Boulevard, St Louis 10, Mo.

**American Board of Ophthalmology.**—The examination of the American Board of Ophthalmology, which was to have been held in Chicago in October, has been postponed until January 1946.

Examinations during 1946 will be held in Chicago, January 18 to 22, in Los Angeles, January 28 to February 1, in New York, in May or June, and in Chicago, in October.

## Book Reviews

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### **A Bibliography of Visual Literature 1939-1944**

Compiled by John F. Fulton, Phebe M. Hoff and Henrietta T. Perkins. Prepared for the Committee on Aviation Medicine, Division of Medical Sciences, National Research Council Acting for the Committee on Medical Research, Office of Scientific Research and Development, Washington, D. C. Price, \$3. Pp. 117. Springfield, Ill. Charles C. Thomas, Publisher, 1945.

In present day warfare the demands placed on the eyes are greater than ever, with special application to the airplane and black-out regulations. Vision has assumed such widespread military importance that the British Air Ministry requested assistance in the compilation of a classified bibliography covering all literature on vision that might have bearing on military operations on land, at sea or in the air. "A Bibliography of Aviation Medicine" was compiled by E. C. Hoff and John F. Fulton, in 1942, and its "Supplement," by P. M. Hoff, E. C. Hoff and John F. Fulton, in 1944. These compilations serve as a pattern for the present volume. In addition to the biologic and psychologic aspects, special attention has been concentrated on physiologic questions concerned with night vision, color vision and perceptual problems. The extensive literature on visual examination and testing of military personnel is fully covered. In the section on therapy, attention is drawn to the newer developments, both surgical and chemotherapeutic, and a separate section on trachoma is added.

The book is extremely useful as a guide to recent literature, particularly as many of the articles abstracted are from other than ophthalmologic journals. Attention, naturally, has been concentrated on the biologic aspects of ophthal-

mology, and the book does not intend to be complete in all phases of general ophthalmology or ocular pathology. It is so well indexed that much time will be saved for any one looking up the literature on a particular subject.

F. H. ADLER

**Refraction of the Eye** By Alfred Cowan, M.D. Second Edition, thoroughly revised. Price, \$4.75. Pp. 278, including index, with 172 engravings and 3 colored plates. Philadelphia: Lea & Febiger, 1945.

The first edition of Dr. Cowan's careful work on "Refraction of the Eye" was published in 1938 and was well received. This second edition, although it contains fewer pages, is really an amplification, since more material has gone into a different format. It is not simply a reprint. Every page has been carefully reviewed, and numerous deletions and additions have been made. Many of the engravings have been improved and clarified. In addition, the chapters have been rearranged to bring relevant and sequential material into closer relationship.

Any one who undertakes the task of writing a book on clinical refraction, particularly if it is to be used as a guide for beginners, faces great difficulties. All necessary optics can be quickly and effectively discussed. But the various methods to be used and solutions to be found for particular difficulties present a formidable array. The evaluation and application of such methods and solutions require not only prolonged practical experience but great aptitude in expression. Dr. Cowan has had the experience and can express himself cogently.

The book can be highly recommended for any one practicing, or intending to practice, ophthalmology.

LEGRAND H. HARDY

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## RESPONSE OF CHRONIC SIMPLE GLAUCOMA TO TREATMENT WITH CYCLODIATHERMY PUNCTURE

FREDERICK W STOCKER, MD

DURHAM, N C

Two types of diathermic treatment have been recommended for glaucoma. In both types the diathermic current is applied to the ciliary region, thus influencing in one way or another that area of the bulbus which is supposed to play an important part in the mechanism for regulating the intraocular pressure. Weve,<sup>1</sup> followed by Amsler,<sup>2</sup> was first to use the surface electrode, a method later emphasized by C H Albaugh and Edwin B Dunphy.<sup>3</sup> The perforating type, called cyclodiathermy puncture, was introduced by A Vogt<sup>4</sup> and developed by him and his associate H Wagner.<sup>5</sup> I had the privilege of attending the meeting at which Vogt made his rather sensational communication. I was at once strongly impressed by the revolutionary idea as well as by the promising results in the most desperate cases of glaucoma. I immediately began to use cyclodiathermy punctures and up to now I have had experience with well over a hundred cases.

Naturally, cyclodiathermy puncture was applied first only in desperate cases of glaucoma which had been unsuccessfully treated by several of the various surgical procedures. In the absence of extensive experience and of observations over a sufficient period of time, some theoretic objections called for conservative use of the method. Especially was the method excluded for chronic simple glaucoma in its uncomplicated form. Albaugh and Dunphy<sup>3</sup> made it clear that cyclodiathermy "is not a substitute for other glau-

coma measures" and in the discussion of their paper Sanford R Gifford emphasized the statement that this is "an operation not for simple glaucoma or for primary glaucoma."

However, as my own experience grew I became more and more convinced that the technic of cyclodiathermy puncture could be so refined as to practically exclude most of the dreaded unfavorable side and after effects. Whereas it is true that one sees many good results with the various operations now in use for glaucoma, there are also many failures. The more I saw of the course of glaucoma, especially in the Negro race, the more it became clear to me that the usual filtering operations, such as trephining, iridencleisis and cyclodialysis, could not be the definite answer to the problem. It must be acknowledged that Iliff<sup>6</sup> demonstrated that not all of the poor results of operations for glaucoma in the Negro are due to racial peculiarity, part are due to the advanced stage of glaucoma when the patients are first seen. Nevertheless I still believe, in agreement with most ophthalmologists who have had experience in treating Negroes for glaucoma, that the beneficial effect of a filtering operation is more likely to be nullified by cicatrization in the Negro than in white persons.

I therefore thought it was justifiable to treat with cyclodiathermy puncture a group of Negroes who were suffering from chronic simple glaucoma and who had not been previously subjected to any other operation. Should the treatment prove to be successful also in that type of glaucoma, and should no unfavorable reactions, side and after effects develop, no one would profit more from this experience than the Negro race.

This report will consist mainly of my experiences with such a group. To my knowledge it is the first time that cyclodiathermy puncture has been reported as being successfully used for uncomplicated chronic simple glaucoma.

It is not my purpose to discuss the theories concerning glaucoma in this paper, which is intended to deal with the problem in an essentially

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<sup>1</sup> Weve, H., cited by Amsler.<sup>2</sup>

<sup>2</sup> Amsler, M., in discussion on Vogt.<sup>4a</sup>

<sup>3</sup> Dunphy, E B., and Albaugh, C H. Cyclodiathermy. An Operation for the Treatment of Glaucoma, *Tr Am Ophth Soc* **39** 193, 1941.

<sup>4</sup> Vogt, A. (a) Versuche zur intraokularen Druckherabsetzung mittelst Diathermieschädigung des Corpus ciliare (Zyklodiathermieschädigung), *Schweiz med Wchnschr* **67** 367, 1937, (b) Cyclodiathermypuncture in Cases of Glaucoma, *Brit J Ophth* **24** 288, 1940, (c) Die Zyklodiathermiepunktur gegen Glaukom, *Klin Monatsbl f Augenh* **103** 591, 1939.

<sup>5</sup> Wagner, H. Diathermieschädigung des Corpus ciliare bei Glaukom, *Schweiz med Wchnschr* **69** 883, 1939.

<sup>6</sup> Iliff, C E. Surgical Control of Glaucoma in the Negro, *Am J Ophth* **27** 731, 1944.

practical way. However, before discussing the mode of action of cyclodiathermy puncture a few words may be said about how the mechanism of stabilizing the intraocular tension may be disturbed in the glaucomatous eye. The increase in intraocular tension characteristic of glaucoma may be brought about either by a blockage of the outflow of the intraocular fluid or by an abnormally increased production of this fluid. In the first case the drainage system is unable to evacuate the aqueous adequately although the latter may be produced in normal quantities. In the latter case the aqueous produced in abnormally large amounts cannot escape through a normal drainage system which would be sufficient in the presence of normal quantities of fluid. Accordingly, the approach to the problem of influencing the balance of the intraocular pressure

The definite answer to the question why diathermy puncture reduces the tension of the eye has not yet been found. Vogt's original idea was that he was to destroy the ciliary body with its processes directly with the coagulating diathermic current. However, when the punctures were applied near the limbus where they reached the corona ciliaris, there was too much reaction and even necrosis of the cornea occurred. It was found that when cyclodiathermy puncture was applied farther back, to the pars plana of the ciliary body, the same result, a lowering of the tension, was obtained. In a specimen from an eye which had been enucleated following severe intraocular hemorrhage, after cyclodiathermy puncture had kept the eye, affected with absolute glaucoma, quiet for more than two years, one may find part of the explanation. Although the



Fig 1—Result of cyclodiathermy puncture when a Vogt needle was used. The illustration on the left shows the untreated side, that on the right, the treated side.

may be either in the direction of increasing the outflow or of decreasing the inflow of the intraocular fluid. Most of the surgical measures for the control of tension in glaucoma, and I shall consider the surgical treatment exclusively in this study, tend to increase the outflow.

Among those procedures which possibly might in part result in an inhibition of the aqueous-producing action of the ciliary body may be mentioned Heine's<sup>7</sup> cyclodialysis, Verhoeff's<sup>8</sup> cyclectomy and Guerry's<sup>9</sup> diathermic obliteration of the posterior long ciliary arteries.

<sup>7</sup> Heine, I. Die Zykliodialyse, eine neue Glaucomoperation, *Deutsche med Wchnschr* **31** 824, 1905.

<sup>8</sup> Verhoeff, F. H. Cyclectomy. A New Operation for Glaucoma, *Arch Ophth* **53** 228, 1924.

<sup>9</sup> Guerry, DuP, III. Angiodiathermy of the Long Posterior Ciliary Arteries and Its Use in the Treatment of Glaucoma, *Am J Ophth* **27** 1376, 1944.

punctures had not reached the corona ciliaris and the ciliary processes directly, they became completely atrophied in the area treated, as can be seen by comparison with the ciliary body of the untreated side of the same eye (fig 1). It must be assumed that by destroying the blood vessels, which are supplied by the long posterior ciliary arteries and reach the corona ciliaris by passing through the pars plana, the circulation of the corona ciliaris becomes impaired to a point at which degeneration and atrophy results. This obviously should ultimately lead to a decrease in production of intraocular fluid. Directly after the application of cyclodiathermy puncture, however, a congestive inflammatory stage may be present which increases the circulation in the whole eye. This also may cause a softening of

the eye but, on the contrary, in some instances, is followed by a temporary rise of tension. I shall come back to that part of the problem later while discussing the results.

As already mentioned, the present study deals with cases of chronic uncongestive glaucoma of various stages that had not undergone surgical treatment in Negro patients. Recently I began to treat with cyclodiathermy puncture also white patients affected with uncomplicated chronic glaucoma. The results seem not to differ from those obtained in Negroes, and I shall later make a more complete report comprising all my experiences.

The patients were treated at Duke Hospital, McPherson Hospital and Lincoln Hospital. The majority were operated on by myself, the rest by the resident house officers, following closely the technic outlined by me.

The group comprises 16 eyes. In each case visual acuity, fields and tension without and with miotics were recorded for some time before the operation. The indication for operation was established as usual, i. e. when the tension could not be kept within normal limits by miotics or when fields and central vision showed signs of deterioration. The number of cyclodiathermy punctures were recorded and a note about the immediate postoperative course made. The tension determined by palpation or taken with the tonometer during the first few postoperative days was carefully watched. Vision, tension and fields were examined at regular intervals and for the purpose of this report the findings when the patient was last seen were recorded. The time of observation varied from one to ten months after the operation.

#### EFFECTS OF CYCLODIATHERMY PUNCTURE

I was interested in finding answers to the following questions:

1. Does cyclodiathermy puncture reduce the tension in simple chronic glaucoma, and if there is a reduction, how long does it last?

2. What influence does the operation have on the whole course of the glaucomatous disease, including vision, field and optic atrophy?

3. Is cyclodiathermy puncture accompanied by complications which would make it appear to be unsuitable for general use as a primary operation in simple chronic glaucoma?

As to the first question one must distinguish between the tension found immediately or a few days after the operation and the tension when last seen. It has been found by previous observers that immediately after cyclodiathermy there is

sometimes not a reduction but, on the contrary, a temporary rise in pressure. This, however, occurs more frequently after surface cyclodiathermy than after cyclodiathermy puncture. In our series, in no case has the tension after the operation been found higher than before. In 1 case it had been unimproved and in another case improved but still higher than normal. In 15 cases the tension was definitely lowered within the first few days after cyclodiathermy puncture. It should be noted that the patients who did not show a satisfactory reduction of tension immediately after the operation were not among those who when last seen had abnormal tension. It would therefore seem that an occasional rise of tension shortly after the operation should have no influence on the final outcome. The period from the operation to the time when last seen naturally varies greatly. Although in a number of cases a much longer time has elapsed since operation the longest time of observation was ten months. Unfortunately some of the patients after they had done well for some time did not continue to present themselves for the regularly scheduled examinations. The tension when last seen was unimproved in no case, improved but still too high in 3 cases, and improved within normal limits in 14. Among those with tension unimproved is included 1 case in which after a second operation the tension was found to be within normal limits.

As to the influence of cyclodiathermy puncture on the glaucomatous process as a whole, including vision, fields and optic atrophy, I think that one should differentiate between the very advanced cases with considerable loss of vision, large field defects and pronounced cupping with atrophy of the optic nerve and the more favorable cases in which the destruction has not yet reached that stage. Arbitrarily I place in the first group patients with central vision of 20/200 or less and marked field defects, and in the second group all patients with vision better than that. In the first group of 8 patients with greatly advanced disease central vision had improved in 2, had become worse in 1 and remained the same in 5. The fields were improved in 2 and the same in 6 cases. In no case did the field show further deterioration. However, in this group there were patients with vision so poor that no fields could be recorded either before or after the operation. If I list these cases as showing no change, this statement does not have much significance. Statistically these cases would have to be eliminated. These patients were among the first ones treated when we cautiously began to try out cyclodiathermy puncture in cases in which there was not

much to lose. In the second group with visual acuity better than 20/200 the central vision had improved in 3, had become worse in 1 and remained the same in 4 cases. The field had improved in 1, became worse in 1 and remained the same in 6 cases.

In 10 cases with the longest period of observation, four, six and one-half, nine and one-half and ten months, the tension was within normal limits in 8, improved but too high in 1 and unimproved in 1 case. Vision was better in 2 cases, worse in 2 and the same as before cyclodiathermy puncture in 6. The fields were worse in 1 case and stationary in 9 cases. As the number of observations is much too small for statistical use, I refrain from giving the results in percentages.

The third question, about complications that might make cyclodiathermy puncture appear unsuitable as a primary operation in chronic simple glaucoma, may be answered favorably as far as our present experience goes. Here again I shall consider the immediate postoperative course separately from the late effects on the eye. A moderate injection, without inflammatory signs in the anterior chamber, was common. Some eyes, however, showed surprisingly little reaction. Moderate reactions with slight irritation of the iris were seen in 2 instances. One patient had fibrinous exudate in the lower part of the anterior chamber, which however disappeared within one week without further complications. Most probably a slight technical mistake produced this accident, as some of the punctures had been placed too far forward in the ciliary body. I shall come back to this observation when discussing the technic. In 2 cases cyclodiathermy puncture was followed by much dispersion of pigment, with numerous deposits of pigment granules on the posterior surface of the cornea. When the patient was seen again after one month these deposits had completely disappeared and the tension was 10 and 13 (Schiotz) respectively. In no case of this series had a hemorrhage into the anterior chamber occurred. This was in contrast with the experience in cases of hemorrhagic glaucoma, in which hemorrhages are not infrequently observed after cyclodiathermy puncture.

While the immediate complications accompanying this operation are negligible, late disturbances were even more conspicuous by their absence. Of course, no case of sympathetic ophthalmia was observed. Although I admit that fears of sympathetic ophthalmia had some theoretic background, the entirely negative experience of all ophthalmologists using cyclodiathermy puncture should lead one to discard this possibility as a serious objection to the method. It

might well be that as the number of operations performed increase sympathetic ophthalmia will occur in rare instances. But certainly there is no evidence that this disastrous disease occurs more frequently after this than after any other operation.

No incidence of infection, either postoperative or so-called late infection, has been observed. Late infection, as for instance that seen after trephining, is not to be expected, as there is no permanent opening left in the bulbus.

The complication I personally dreaded most was cataract, and I watched the lens in these cases for months with some anxiety. Careful study with slit lamp and ophthalmoscope was carried out every time the patient was seen. I state positively that no opacities which could be attributed to cyclodiathermy puncture were ever observed. I could not even see senile opacities progress faster than expected after the operation. The fact that the vision in general was well preserved during the months of observation after cyclodiathermy puncture is in line with this statement. However, I believe that it is wise for any one who wishes to use cyclodiathermy puncture to follow certain principles of technic in order to be safe. I shall come back to this point.

Friedenwald in discussing Dunphy's<sup>3</sup> paper raised the question about accommodation, astigmatism and gonioscopic appearance of the angle of the chamber. The accommodation could not be determined accurately because of the advanced age of most of the patients. So far as astigmatism is concerned I made one peculiar observation. In 1 case a patient who required a correction of  $-75\Delta$  cylinder, axis 180 before the operation saw definitely better with the same cylinder, axis 90 a few weeks after the operation. Gradually he came again to require a sphere, and when last seen he took the same lens and the same axis as before cyclodiathermy puncture. I record this observation, however, I am hesitant to interpret it as definitely connected with the operation.

Gonioscopic observations were not carried out routinely, but no specific influence on the angle of the chamber was observed when it was used. However, one had the impression that the chamber in some cases had become slightly deeper.

A peculiar change in the pupil occurred in some cases. It remained slightly larger than before the operation, sometimes it was not quite exactly round as before and reacted sluggishly to light. This may have some relation to the disturbed innervation or may be caused by slight diffuse posterior synechia following a mild postoperative irritation.

After considering in detail all observations made after cyclodiathermy puncture it may positively be said that no side or after effects could be observed which would make this operation appear to be unsuitable as a primary operation for chronic simple glaucoma.

#### TECHNIC

A careful choice of technic is essential for successful results from cyclodiathermy puncture and the avoidance of complications. The ultimate goal must be to cause the least harm to the eye while producing maximum action against the glaucoma, i. e., there must be a permanent stabilization of the intraocular tension within normal limits.

A very fine and short needle must be used. Vogt's needle, 0.5 mm long and 0.18 mm in diameter, or the shortest type of Kronfeld's needle may be satisfactory. More recently I have been using exclusively a needle that has been made according to my own suggestions. It is better insulated and may be recommended.<sup>9a</sup> Very little current should be used. Vogt used to recommend 60 milliamperes. However, I found that it was



Fig 2—Result of cyclodiathermy puncture when Walker micropins were used. Arrow shows herniation of ciliary body into sclera.

not practical to rely on a milliamperage meter and that it was necessary to determine at the beginning of the operation how much current is necessary to just produce coagulation on the surface of the sclera. Usually the Walker machine is set between 15 and 20.

The importance of a proper needle is made clear in comparing figures 1 and 2. In the first

case a Vogt needle was used and in the second case one of the so-called Walker micropins made of platinum. In the first case the structure of the sclera as a whole was left intact. There was some hyperplastic scar tissue comprising the posterior part of the ciliary body. In the second case the effect was too destructive, resulting in a defect in the sclera into which part of the ciliary body herniated. This, of course, is not desirable.

The question then arises how many punctures should be made and how large an area has to be covered. The area to be covered can be seen in figure 3. It shows the relative location of the

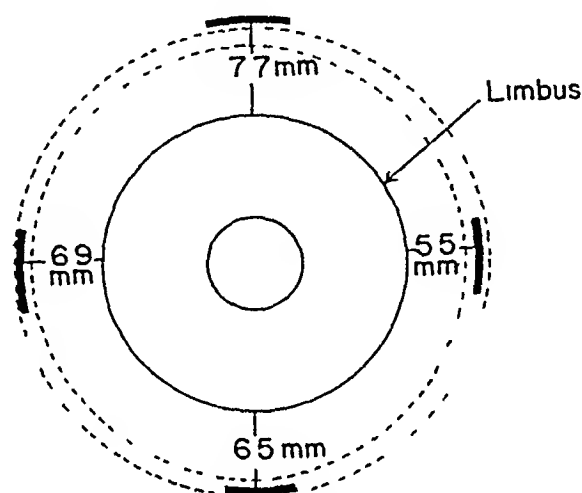


Fig 3—Area to be covered by cyclodiathermy puncture. The four wide black spaces indicate the distance from the limbus of the insertions of the rectus muscles. The parallel circles of broken lines indicate the distance from the limbus of the ora serrata, which is variable—5 to 7 mm on the internal side and 6 to 7.5 mm on the external, inferior and superior side.

insertions of the recti muscles after E. Fuchs<sup>10</sup> and of the ora serrata according to Wagner's<sup>5</sup> findings. An area beginning from 2.5 to 3 mm from the limbus to the ora serrata should be covered. Therefore on the inner side the punctures must extend back somewhat farther than the insertion of the internal rectus, on the inferior side just about beyond the insertion of the inferior rectus, and the same distance on the external side. If the punctures are applied to the upper part of the globe they should not extend quite as far as the insertion of the superior rectus. The coagulation needle should be left in the sclera a little longer than one second. I count 1, 2, 3 during the procedure. On the count of 1 I introduce the needle, on 3 I remove it. The needle should be under current throughout the procedure. Usually somewhat more than one third of the inferior circumference is treated. We tried to establish a relation between the number of millimeters of mercury of tension and the

<sup>9a</sup> This needle is manufactured by V. Mueller & Co., 408 South Honore Street, Chicago 12, Ill.

<sup>10</sup> Fuchs, E. Beitrage zur normalen Anatomie des Augapfels, Arch f. Ophth. 30 (pt 4) 1, 1884.



number of punctures We are tentatively following the formula number of millimeters of mercury of tension plus 30 equals the number of punctures required However, never more than 80 punctures should be applied in chronic simple glaucoma

#### SUMMARY AND CONCLUSIONS

1 Cyclodiathermy puncture as far as my experience with 16 cases of chronic simple glaucoma goes has proved to be a harmless procedure as deleterious complications have not developed in any case

2 Its influence on the tension and the general course of the disease is generally beneficial

3 The lowering of the tension is of long duration, and there is much hope that by refining the technic and repeating the procedure when necessary permanent stabilization of the intra-

ocular tension may be achieved even in those cases which show a tendency toward rise of tension after a certain time

4. Cyclodiathermy puncture has certain definite advantages over other operations used for glaucoma simplex It seems to work regardless of the type of glaucoma No late infection is to be feared No tendency toward stimulating the development of opacities of the lens can be demonstrated No rapid deterioration after the operation in advanced cases, as frequently seen in some of the other procedures, occurs It therefore may be applied safely in all stages of chronic simple glaucoma

5 As shown in this study cyclodiathermy puncture is effective also for the Negro and may well become the method of choice for the treatment of the severe disease in this race

6 A careful observation of the technic as outlined is essential

# DIABETIC RETINITIS

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## CHANGES IN FUNDUS OF EYE ASSOCIATED WITH DIABETES

The changes which are seen in the fundus of the eye in cases of diabetes may be classified as follows

- I Diabetic retinitis, or retinopathy proper
  - 1 Small, round and irregular hemorrhages
  - 2 Sharply defined, white exudates in the deeper layers of the retina
  - 3 Yellowish white, glistening deposits
- II Complicating elements in the ophthalmoscopic picture due to changes in the retinal vessels
  - 1 Changes due to aging and arteriosclerosis irregular tortuosity of the vessels, irregularity of the lumen, widening of the light reflex apparent compression of veins where crossed by arteries
  - 2 Changes due to contraction of small vessels in the course of the later stages of essential hypertension a few small irregular hemorrhages and an occasional cotton wool patch
  - 3 Changes due to obstruction of a large branch of the central vein hemorrhages of all sizes in a sector of the fundus
  - 4 Changes due to episodal arteriospastic retinopathy in the course of the later stages of essential hypertension edema of the retina and of the optic disk, cotton wool patches, other exudates and hemorrhages of all shapes and sizes
- III Changes found only in some cases of severe diabetic retinitis
  - 1 Large, massive hemorrhages in the retina and in the vitreous
  - 2 Proliferation of numerous new vessels with connective tissue formation in the retina and in the vitreous

These various hemorrhages and exudates seen in the fundus of the eye present the first problem, that of diagnosis. What constitutes diabetic retinitis, or retinopathy proper? It is obvious

that the changes in the vessels and the hemorrhages and exudates secondary to them which I have placed in group II cannot be due to diabetes. Aging and arteriosclerosis of the retinal vessels occur in advanced age in nondiabetic persons. Contractions of small vessels, obstruction of vascular branches and episodal arteriospastic retinopathy occur in the later stages of essential hypertension in persons without diabetes. The hemorrhages and exudates which are the result of such changes are, therefore, not due to the diabetes. However, diabetes is foremost a disease of middle and advancing age and so is essential hypertension and both diseases are of frequent occurrence. It is natural, therefore, for these vascular changes and their consequences to occur in the course of diabetes, but there is not necessarily any causal relation between such changes and the diabetes. Moreover, these changes do not occur in young diabetic patients who do not have essential hypertension and do not show aging and arteriosclerosis of the retinal vessels. The only problem that these vascular changes present in relation to diabetes is the relative frequency of their occurrence in diabetic and in nondiabetic persons. I know of no satisfactory statistics which give the relative frequencies of arterial hypertension, aging and arteriosclerosis of the retinal vessels, contractions of small vessels, obstruction of branches of the retinal vessels and episodal arteriospastic retinitis in the various age groups of diabetic and of nondiabetic persons. Such statistics, if they are to have any value, will have to include large groups of cases and will have to consider the various degrees of severity of the diabetes and its duration, and a number of other factors. So far no such statistics are available.

*Diabetic Retinitis or Retinopathy*—With the elimination of the vascular changes, there are left the hemorrhages and exudates in group I (1) small, round and irregular hemorrhages, (2) sharply defined, white exudates in the deeper layers of the retina, and (3) yellowish white, glistening deposits.

The hemorrhages are situated mainly in the area between the upper and the lower temporal vessels of the retina and in the region surrounding the optic nerve head and may extend to the

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periphery Most of these hemorrhages are small, round and deeply situated, but superficial radial and irregular hemorrhages are also seen The exudates are small and white, with sharp margins They are discrete or confluent, forming all kinds of figures, including circinate ones They are situated in the deep layers of the retina behind the retinal vessels Their pathologic substratum is a deposit of hyalin mixed with lipid The glistening, yellowish white exudates vary in size from a pinpoint to large irregular masses and are due to accumulations of cholesterol

The small, round and deep hemorrhages constitute the most characteristic feature of diabetic retinitis They do not stand in any relation to the complicating vascular changes of group II In their characteristic form they occur only in diabetes, and in no other disease that I know of When these hemorrhages are seen in the fundus of the eye, diabetes can be assumed to be present in practically every case When the small white exudates and the glistening deposits are also seen, the complete picture of diabetic retinitis is present This characteristic picture does not occur in any other disease It is found not only in middle-aged and elderly but in young diabetic patients and may be present without any complicating vascular changes In the discussion following the presentation of this subject by Dr Sanford Gifford before the New York Diabetic Association in 1943, one of the speakers said that "retinal hemorrhages are found in some persons who are perfectly normal in every other respect" This is not so Retinal hemorrhages are always pathologic, and small, deep and round hemorrhages are found only with diabetes The relative frequency with which they are found in diabetic persons varies with the different investigators Waite and Beetham<sup>1</sup> found deep retinal hemorrhages in 18 per cent of 3,915 visible fundi The percentage varied with the duration of the diabetes, from 57, when the duration was only one year, to 589, when the duration was over fifteen years I venture to state that the frequency would be still higher were the tiny hemorrhages more diligently sought for As a feature of diabetes the ophthalmoscopic picture is of importance, for it is at times found on routine examination when the hyperglycemia is still below the threshold level for the excretion of dextrose in the urine

*Severe Retinal Complications*—I have placed the changes which complicate some cases of diabetic retinitis in group III First of these are

the retinal and preretinal large, and even massive, hemorrhages, which occur repeatedly and rupture into the vitreous They do not occur in all cases of typical diabetic retinitis but appear only in a limited number Such hemorrhages quickly destroy vision They are difficult of absorption, and they are sometimes replaced by retinitis proliferans Such hemorrhages arouse the suspicion that diabetes is present, even when they do not allow a good view of the fundus They nullify the good results of a cataract extraction properly performed

The second complication appears only in a small number of cases of diabetes, but it occurs only in this disease and is characteristic of it There are seen in the fundus numerous fine, newly formed vessels covered by a thin, delicate, veil-like connective tissue The vessels, with their covering of connective tissue, project into the vitreous in brushlike form or intertwined in various configurations In a case seen at the New York Eye and Ear Infirmary the veil of tissue projected into the vitreous for about 8 D and contained within its meshes a fine network of vessels This formation of new vessels and connective tissue occurs without massive hemorrhages into the vitreous and differs in appearance from the proliferating connective tissue which follows the partial absorption of a hemorrhage in the vitreous Although a number of such cases have been seen at the New York Eye and Ear Infirmary, their occurrence is not frequent Hanum's<sup>2</sup> article contains excellent colored illustrations, and in Klien's<sup>3</sup> there are photographs and drawings showing the development of these vessels and their connective tissue support

#### PATHOGENESIS OF DIABETIC RETINITIS

The second problem of diabetic retinitis is that of the pathogenesis of the small round hemorrhages, of the exudates, of the massive hemorrhages which rupture into the vitreous and of the new formation of vessels The pathogenesis of the exudates is perhaps the easiest to explain Deposits of hyalin and lipid occur in any tissue which suffers from insufficient nutrition and inadequate oxygen supply Such a condition must be present in the retina in the areas where the exudates are found Primarily the concern is with the small, deeply situated, round and irregular hemorrhages There is no doubt that these hemorrhages occur by diapedesis through the

<sup>1</sup> Waite, J H, and Beetham, W P The Visual Mechanism in Diabetes Mellitus, New England J Med 212 367 (Feb 28), 429 (March 7) 1935

<sup>2</sup> Hanum, S Diabetic Retinitis, Acta ophth, 1938 supp 16, p 3

<sup>3</sup> Klien, B A Retinitis Proliferans Clinical and Histologic Studies, Arch Ophth 20 427 (Sept) 1938

walls of the capillaries. The question is: What is there in diabetes which causes small hemorrhages by diapedesis into the retinal tissue?

There are certain well defined principles in pathology concerning the passage of blood through the capillary wall. When, for any reason, the capillaries are dilated, with a contraction or relative narrowing of the artery above, there is slowing of the blood flow in the capillaries, a condition of *prestasis*. The capillary wall becomes soft, openings form in it which permit the passage of red blood corpuscles, and these openings then close. Small hemorrhages in the retina, such as are typical of diabetic retinitis, can occur only in this manner. That there is in the retina a chronic *prestatic* condition, with slowing of the circulation in the capillaries, is also shown by the hyalin and lipids, which indicate a disturbed nutrition of the retinal tissue. The question then is: What is there in diabetes which causes a *prestatic* condition in the capillaries of the retina with resulting small hemorrhages?

There are a number of elements in the occurrence of the small hemorrhages of diabetic retinitis which must be kept in mind. They occur in young, as well as in middle-aged and old, persons. They have no relation to the vascular changes enumerated in group II. They occur with severe diabetes, as well as with the mild form. In fact, they occur frequently with long-standing mild diabetes, and they are at times discovered before the presence of glycosuria is known to the patient. If, therefore, one is to relate the *prestatic* condition of the retinal capillaries to the diabetes, it is the mild form of diabetes which one must consider—the moderate hyperglycemia, with slight secondary nutritional changes and without the terrific depletion of carbohydrate in the liver which results in secondary metabolic changes. How does a patient with such a mild form of diabetes differ from a normal person?

As I understand it, diabetes is a condition in which the organism is unable to maintain the normal blood sugar level, which is approximately 80 to 90 mg per hundred cubic centimeters. If the maximum upper limit of normal is considered as about 110 mg, a continuous blood sugar level above this value, say from 130 to 160 mg, with or without glycosuria, constitutes mild diabetes. In a case of diabetes of this type, the lability of the blood sugar level is greater than normal, and the dextrose tolerance curve after the ingestion of carbohydrates is characteristic of diabetes. It is in such a case that the typical small hemorrhages are likely to occur. It must be remembered

that in such a case, before the diabetes is even accidentally discovered, many years have passed, with the level of dextrose in the blood rising only gradually to 120, 140, 150 and 160 mg per hundred cubic centimeters, until eventually glycosuria is noted. A patient with such a moderate degree of hyperglycemia differs in no manner from a nondiabetic person save in the lessened ability to regulate the blood sugar level. It is, therefore, in my opinion, the continuous moderate hyperglycemia lasting over years which stands in some causal relation to the production of a *prestatic* state in the capillaries with the resulting small hemorrhages. This is as far as I can go in attempting to explain the pathogenesis of diabetic retinitis. And this is as far as any one can go unless one would rather assume as a cause of the hemorrhages the presence of toxic substances which cannot be found or a deficiency of unknown vitamins, which so far have not been discovered, or attribute the hemorrhages to some of the vascular conditions mentioned in group II, which obviously have nothing to do with the typical hemorrhages of diabetic retinitis.

The attempt to relate causally the continuous moderate hyperglycemia to the hemorrhages of diabetic retinitis does not, of course, solve the whole problem of the pathogenesis of diabetic retinitis. Just how the hyperglycemia produces the *prestatic* condition in the capillaries of the retina I do not know. There also remains the question why the hemorrhages are not found in every case of diabetes, although they are probably present more frequently than any statistics indicate.

On the supposition that the hyperglycemia is the responsible factor, the massive hemorrhages which rupture into the vitreous can be assumed to be due to an aggravated form of *prestasis*. But why such an aggravated form occurs in only a limited number of cases of diabetic retinitis I do not know.

There still remains the necessity of explaining the occurrence of the newly formed vessels in some cases of diabetic retinitis. I know of no satisfactory explanation, unless perhaps the slowing of the circulation in a large number of capillaries at one time and in one area supplies the stimulus for the formation of new vessels.

#### TREATMENT OF DIABETIC RETINITIS

The third problem of diabetic retinitis is that of treatment. I know of no means which will prevent the occurrence of retinal hemorrhages in cases of diabetes or cause them to disappear when they have occurred. Usually the ophthalmologist

advises that the patient submit to a careful regimen of diet and insulin prescribed by his attending physician. Most ophthalmologists feel that the blood sugar should be kept as close to the normal level as possible. However, it is doubtful whether it is possible by any means to keep the blood sugar of any diabetic patient at the normal level of 80 to 90, or even 100 mg per hundred cubic centimeters. Most physicians are quite satisfied when the blood sugar can be kept at about 130 to 150 mg. This level represents still a continuous mild hyperglycemia, just the condition which I think is responsible for the prestatic condition in the capillaries of the retina, with the resulting hemorrhages.

#### SUMMARY •

Diabetic retinitis, or retinopathy, is an easily recognizable ophthalmoscopic entity characterized by small, round and irregular hemorrhages, sharply defined, white exudates in the deeper layers of the retina due to hyalin and lipids, and yellowish white, glistening exudates, due to deposits of cholesterol.

The ophthalmoscopic picture is at times complicated by changes in the retinal vessels and their consequences, such as aging, arteriosclerosis, contraction of small vessels, obstruction of a venous branch and episodal arteriospastic retinopathy. There is no causal relation between these changes and those of diabetic retinitis.

Some of the cases of severe diabetic retinitis are characterized by large retinal hemorrhages which rupture into the vitreous. A few cases are also characterized by the proliferation in the retina and the vitreous of newly formed vessels which are covered by a connective tissue layer. This form of retinitis proliferans differs in its appearance and its genesis from the retinitis proliferans following the partial absorption of a hemorrhage in the vitreous.

It is my opinion that in its pathogenesis diabetic retinitis stands in close relation to the continuous hyperglycemia which is in all probability responsible for the condition in the capillaries resulting in hemorrhages.

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# REVALUATION OF HERBERT'S FLAP OPERATION FOR GLAUCOMA

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Lieutenant Colonel H. Herbert<sup>1</sup> of the Indian Medical Service contributed many splendid articles on the surgical treatment of glaucoma from 1903 to 1934. Like most ophthalmic surgeons of his day, he expressed himself in positive terms, stating at each writing that he had found a final solution for the treatment of glaucoma. A review of his contributions indicates that he discarded one discovery for another, leaving the reviewer with the impression that his accumulated experience compelled him to change his technic. He was one of the early pioneers advocating the use of the iris inclusion operation. But one of the outstanding methods which he so colorfully described as a future cure for glaucoma seems to have been abandoned in favor of more popular methods.

It is my purpose to rededicate his well known trapdoor or flap operation devised initially for



Fig 1—A narrow Graefe knife

absolute glaucoma. In the *Transactions of the Ophthalmological Society of the United Kingdom*, of 1907 and 1910, Herbert described a rectangular trapdoor operation having as its basic principle the drainage of fluid from the interior of the eyeball through an opening in the sclera, in the anterior segment, to the subconjunctival space. Using a narrow Graefe knife (fig 1), he made an incision in the sclera 2 mm long and about 1.5 mm from the corneal margin in the lower outer quadrant of the globe (fig 2). From the two ends of this small incision, two shorter forward cuts were made to the limbus by turning the edge of the same narrow blade forward and sawing carefully to avoid puncturing the iris, in the emptied anterior chamber. He thus created a small rectangular flap or

tongue of corneoscleral tissue, which was cut subconjunctivally with its base at the limbus (fig 5). At a later period, Herbert repeated this operation in the upper outer quadrant of the eye (fig 6). In a later report he moved the sclerotomy opening to the midline (fig 4).

In his various reports, one is impressed by the many changes in the technic of performing this simple operation. For those who are in-

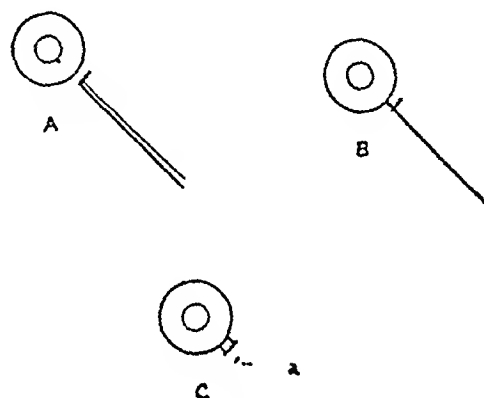


Fig 2—The earlier operation, a, conjunctival puncture

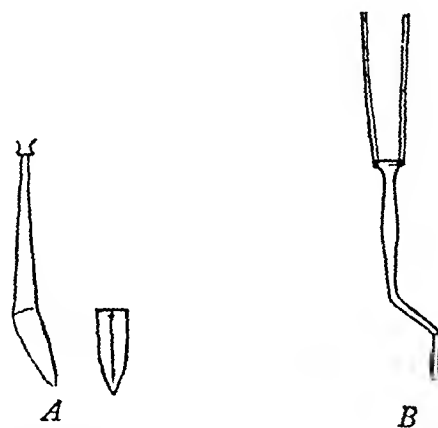


Fig 3—A, Syms iridectomy knife, B, Taylor's cataract knife, modified

terested in historical aspects, I refer to the original articles.

Regardless of the instruments used (fig 3) and the delicate technic involved, there stands out conspicuously the underlying principle of the operation, namely the utilization of the trapdoor in the sclera which would serve as a continuous but slow drainage ditch siphoning the aqueous from the anterior chamber to the outside of the eye, under the conjunctiva.

Read at the meeting of the College of Physicians, Philadelphia, Section on Ophthalmology, March 15, 1945

<sup>1</sup> Herbert, H. *Tr Ophth Soc U Kingdom* 23, 324, 1903, 39 220, 1919, 41 239, 1921, *Ophthalmoscope* 5 292, 1907, 9 76, 1911, 11 398, 1913, *Brit J Ophth* 4 216 and 550, 1920, 5 183 and 417, 1921, 14 433, 1930, 18 142, 1934



Colonel Herbert reports the result of his trapdoor operation on eyes already blinded by glaucoma. He claimed that he obtained good results in 5 cases out of 7.

Reading between the lines of his reports, I must deduce that he was satisfied with the term good result when he secured a reduction in the tension in absolute glaucoma without restoration of vision. He expressed the thought that the principle of the trapdoor operation might well be applied in the operation for primary glaucoma. It was this expression of opinion,

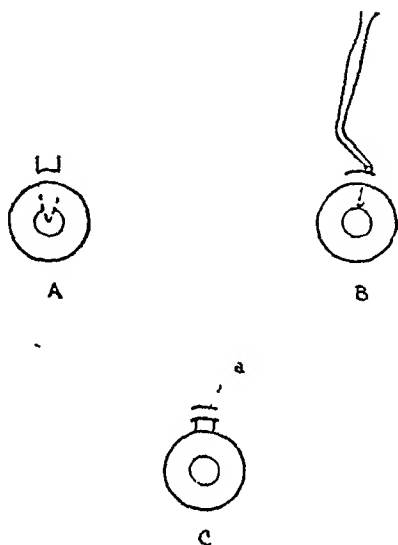


Fig 4—The "small flap" operation, a, conjunctival puncture

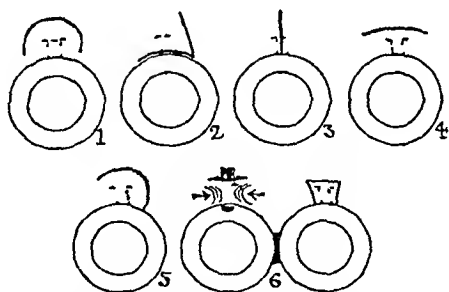


Fig 5—Various conjunctival incisions for Herbert's sclerotomy

coupled with the rational hypothesis underlying the principle of this operation, that enticed me to pick up the threads where he left off.

I, too, like Herbert, operated in 7 cases in which the eyes were blinded by glaucoma, 2 of them secondary glaucoma, resulting from long-standing uveitis, and the remaining 5 primary glaucoma in the final stages of absolutism.

#### A MODIFIED TECHNIC OF TRAPDOOR OPERATION FOR ABSOLUTE GLAUCOMA

The technic is described as follows. An incision is made in the conjunctiva 8 mm from the limbus. The conjunctiva is dissected in the

same manner as when preparing for an Elliot trephine. Just 2 mm below this point of incision, a scleral cut is made with a Graefe knife at least 4 mm in length. The site of this incision need not be exactly at 12 o'clock but in a selected area where the anterior perforating ciliary vessels are least prominent. If the episcleral vessels cannot be avoided, then they must be sacrificed for the sake of the scleral incision. Several determined movements of the cataract knife may be necessary before the sclera is perforated. One need not fear the result of cutting the uveal elements beneath the sclera. Should they be cut inadvertently, no harm will result. At one end of the scleral incision, a blade of a sharp pointed scissors is entered between the sclera and the uveal coat while the other blade is on the sclera. A cut is made 2 to 3 mm toward the cornea at an angle of 90 degrees. A similar cut is made at the opposite end of the scleral incision. The eye being under tension, there is an immediate prolapse of black uveal tissue. A spatula is then placed into the eyeball through

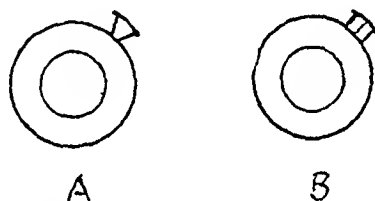


Fig 6—Modifications in the "small flap" operation

the trapdoor opening and directed toward the anterior chamber in exactly the same manner as a cyclodialysis. While the spatula is still in position it may be sufficiently depressed to allow escape of aqueous through the trapdoor. Following the removal of the spatula the conjunctival wound is closed by a continuous silk suture.

Instead of making a single trapdoor, a double sclerotomy may be performed, one in the upper nasal aspect and the second in the upper temporal aspect. Such a double opening is desirable in glaucoma in which the intraocular tension is very high and is attended by excruciating pain. The single trapdoor may be reserved for those cases in which light perception has been retained, and there exists hope of obtaining some restoration of vision, even though it be very slight.

I shall here report 2 cases in which the operation was used and which are very impressive.

#### REPORT OF CASES

CASE 1—R. B., a woman aged 25, in 1940 had papillitis of the left eye from which she presumably recovered. In 1941, examination revealed a postpapillitic optic atrophy of the same eye. In January 1944, she con-

sulted me because of pain in the left eye with gradual loss of vision. The intraocular tension of both eyes was 40 —, visual acuity in the right eye was 5/5, and of the left eye, questionable light perception. There were the usual signs of chronic congestive glaucoma of the inflamed left eye with exacerbations of acute symptoms and glaucoma of the right eye with good vision, with changes in the fields characteristic of glaucoma.

Under miotics, the tension of the right, seeing eye was reduced to 21.5. In the left, blind eye the tension was 47, light perception was lost. With the development of absolute glaucoma in the left eye, pain became unbearable. The patient refused enucleation. A double Herbert operation was performed on April 3, 1944, one on the temporal and one on the nasal portion of the globe associated with cyclodialysis. There was complete cessation of pain, and the tension dropped to 15.

CASE 2—E. B., a woman aged 49, in 1939 consulted me because of anterior uveitis of the left eye associated with pain and an intraocular tension of 35. Visual acuity was light perception. The tension of the fellow eye was 19, the visual acuity being 5/30 corrected by glasses to 5/9. She claimed that eleven operations had been performed on the sightless eye by the late Dr. L. Webster Fox over a period of years, temporary relief being obtained after each operation.



Fig 7—Trapdoor operation for absolute glaucoma. The sclerotomy is shaped like a staple, as shown in the artist's conception portrayed in the illustration.

A Herbert flap operation was performed Dec. 13, 1939 on the left, blind eye at a point 8 mm from the limbus close to the insertion of the superior rectus muscle. A large trapdoor was made measuring 6 mm horizontally and 4 mm in a vertical direction at the extreme ends of the scleral incision. There was thus produced a U-shaped opening in the sclera through which uveal tissue extruded. The conjunctiva was closed in the usual manner over the trapdoor. The tension was gradually reduced, the last on record being 17 in the left affected eye on Dec. 8, 1944. The visual acuity with a minus 6.5 lens was 5/30. An area of chorioretinal atrophy in the inferior temporal quadrant was noted.

In this instance, the Herbert operation succeeded in establishing a point of drainage between the uveal coat of the eye and the subconjunctival space. It is now known that the patient had an acute localized chorioiditis associated with secondary glaucoma. It is also now known that the Herbert operation established an avenue of escape for accumulated fluids from the posterior segment of the eyeball.

I am presenting also a photograph (fig. 7) of the eyes of a patient who refused surgical inter-

vention for chronic congestive glaucoma. Only when he became totally blind, and the right eye became painful did he submit to surgical procedure. A Herbert operation was performed on the right eye which still had light perception. He now has light perception with marked reduction in intraocular pressure, the record of Nov. 14, 1944 being: right eye, tension 25, left eye, not operated on, 41.

#### CONCLUSIONS ON HERBERT OPERATION

I am satisfied that enucleation should be performed on all painful blind eyes associated with increased intraocular pressure. There are circumstances in which the patient does not agree to surgical removal. Only in those instances in which blindness results from chronic uveitis or as a result of a primary glaucoma do I believe that the Herbert operation should be performed to relieve pain and to satisfy the patient's whim of retaining a dead eyeball.

#### POSSIBILITIES OF HERBERT'S FLAP OPERATION

Herbert proposed that the trapdoor operation may be effective in all cases of primary glaucoma. That was in 1910. In later publications, 1920 and 1921, he reported that he and his associates performed the sclerotomy for primary and secondary glaucomas as it was introduced in 1907. He concluded that the sclerotomy was valuable when miotics failed to hold the tension. In 1934, he reported a series of iris inclusion operations, indicating that the anterior sclerotomy had failed to serve his purpose in all cases.

I believe, however, that Herbert was persuaded by the popularity of iris inclusion operations. In reviewing the various types of operations for glaucoma, principally the primary type, I find that Herbert did make an extremely important contribution in the small flap operation. I am speaking, however, of the principle underlying the operation rather than of the surgical procedure itself. I find that this principle may be further modified by moving the area of sclerotomy to a point corresponding to and beyond that space in the sclera covering the ciliary body.

At present, the common location for operation for glaucoma is limited to the corneoscleral margin at a point where the canal of Schlemm has already been occluded and at the point where serious accidents occur by the operation itself.

If one were to accept the theory that acute and chronic congestive glaucoma are attended by enlargement of the ciliary body and a swelling of the entire choroid coat, then one must also accept the hypothesis that the pathologic process

in the anterior segment of the eye in the region of the canal of Schlemm, with all its implied connections of iridocorneal disease, and the general advancing of all the ocular tissues forward are the result of the increased fluid content of the vitreous chamber segment

If, again, the origin of acute glaucoma is in the vitreous chamber segment, it seems equally logical that the new exit of fluids should be made in the silent portion of the eyeball, rather than at the corneal margin

The same holds true for chronic simple glaucoma which has as its basic pathologic conditions arteriosclerosis and fibrosis of the tissues of the eyeball. If one holds to the theory that the canal of Schlemm is so sclerosed and fibrotic that it is no longer an exit for fluids then it is likewise true that the new exit for these fluids should not be in the obstructed angle but in the silent areas of the eyeball

Herbert originally made his anterior sclerotomy 1.5 mm from the limbus. Later, he agreed to advance it to 2, 3 and 4 mm. My contribution to the Herbert operation is a further shifting of the exit in the sclera 4 to 8 mm from the limbus, producing a trapdoor in the region of the eye corresponding to the location of the ciliary body and immediately beyond, where the fluids are excreted and where they may be

evacuated at their source. This area is approximately 6 mm from the limbus. It is my opinion that the Herbert operation can be reenforced in value if performed at a new location situated away from the dangerous area of the eye which has already been damaged by increased pressure. The operation can be performed without serious trauma and certainly without the complications common to the trephine, inclusion operations and basal iridectomy. The trapdoor is not a fistulous opening. It is closed with a layer of uveal tissue which is noted as a black U-shaped area beneath the conjunctiva. This uveal tissue acts like spongy weather stripping through which fluids are exchanged between the inside and the outside of the eyeball. It serves as a wick just as in the iris inclusion operations. The operation can be repeated at different locations should ocular tension return.

Of course my experience is limited to 2 cases of uveitis and to 5 of absolute glaucoma. Until I have been able to report convincingly on the trapdoor operations in early primary glaucoma, I must hold my judgment in abeyance. However, ideas must precede performance. I am presenting Herbert's principle of the trapdoor operation, some distance away from the corneoscleral margin, as an idea for future guidance in the surgical treatment of primary glaucoma.

# PENETRATION OF PENICILLIN INTO THE EYE

## FURTHER STUDIES

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Studies by Struble and Bellows<sup>1</sup> and Leopold and LaMotte<sup>2</sup> on the penetration of penicillin into the eye after topical and systemic use were carried out with commercial preparations, and the concentrations obtained in various parts of the eye were expressed in Oxford units. A direct comparison of their results and those published by this laboratory<sup>3</sup> is not possible, since in our experiments a relatively crude preparation of penicillin was applied. The strain of *Penicillium notatum* used was grown in the medical department of the Presbyterian Hospital under the supervision of Dr Gladys Hobby and extracted in the laboratory of Dr Karl Meyer, of the Department of Ophthalmology, titration according to the Oxford method was not done. In the same study, the penicillin activity in the aqueous and vitreous fluids was determined by means of the Fleming dilution method, and the concentrations were given in micrograms of penicillin per cubic centimeter. Although the results clarified the relation of the three types of topical application in the rabbit's eye, it was thought advisable to repeat and to extend several series of experiments using solutions of commercial salts and to estimate the penicillin activity of the ocular fluids by the Oxford cup method and the Fleming dilution technique, and that of the tissues of the eye by the Oxford cup method. The

determinations of penicillin in the latter tissues were made in conformity with the work of Struble and Bellows. Three local methods, designed to introduce comparatively high concentrations of drugs in the anterior segment of the eye, were tested on rabbits and the results compared: subconjunctival injection, iontophoresis and the application of cotton packs saturated with a solution of penicillin. The penetration of penicillin into the human eye after two types of topical application was estimated in several suitable cases to procure information on the extent to which the results of experiments on rabbits are applicable to the human eye.

### SUBCONJUNCTIVAL INJECTION

*Technic*—One-half cubic centimeter of a solution of commercial sodium penicillin containing 5,000 Oxford units of penicillin per cubic centimeter was injected subconjunctivally. After local anesthesia with 0.1 per cent nupercaine hydrochloride, half the amount was injected beneath the upper part of the bulbar conjunctiva and the remainder beneath the lower part. One, two, four and six hours later, aqueous and vitreous fluids were withdrawn, the cornea and the iris with the ciliary body were dissected at the one, two and four hour intervals. The amount of penicillin in the aqueous was generally determined in appropriate dilutions by means of the Oxford cup and Fleming dilution methods. The cornea and the iris with the ciliary body were weighed and ground with ignited quartz sand and a phosphate buffer solution ( $pH$ , 6.7 to 7.0) which was also used for the washing of the mortars, pestles and weighing bottles. The extracts and washings were combined in a centrifuge tube and diluted to twenty times the weight of the respective tissue. The tubes were centrifuged, and quadruplicate samples of the supernatant fluid were used for the determination of penicillin by the Oxford cup method. Whenever possible, the samples were kept on ice during the various steps of processing. Each experiment was repeated three to eight times.

*Results*—The subconjunctival accumulation of fluid was commonly yellow one hour after the injection. At this time the amount of penicillin in the aqueous (table 1) varied from 0.75 to 1.0 Oxford unit per cubic centimeter as determined by the dilution method and from 0.68 to 1.4 Oxford units per cubic centimeter as determined by the cup method. The averages for the two types of determination were in close agreement, 0.91 and 0.93 Oxford unit, respectively, per

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The penicillin for these experiments was released by the Committee on Therapeutics and Other Agents, Division of Medical Sciences, National Research Council. Preparations from two large pharmaceutical companies were used.

1 (a) Struble, G. C., and Bellows, J. G. Studies on the Distribution of Penicillin in the Eye and Its Clinical Application, *J. A. M. A.* **125**: 685 (July 8) 1944.  
(b) Bellows, J. G. Penicillin Therapy in Ophthalmology, *Am. J. Ophth.* **27**: 1206 (Nov.) 1944.

2 Leopold, I. H., and LaMotte, W. O., Jr. Penetration of Penicillin in Rabbit Eyes with Normal, Inflamed and Abraded Corneas, *Arch. Ophth.* **33**: 43 (Jan.) 1945.

3 von Sallmann, L., and Meyer, K. Penetration of Penicillin into the Eye, *Arch. Ophth.* **31**: 1 (Jan.) 1944.

cubic centimeter The vitreous fluid exhibited a slight degree of penicillin activity in 1 of 5 instances The figures for the cornea are given in Oxford units per gram wet weight The penicillin content of the individual corneas ranged from 6 to 12 per cent of the average given in the table for 1 Gm wet weight The quantity of penicillin in the corneas varied from 32.8 to 75.5 Oxford units, with an average of 53.2 Oxford units, per gram wet weight The iris with the ciliary body also showed variations in penicillin content, that is, from 7.1 to 23.1 Ox-

TABLE 1—Concentration of Penicillin in the Aqueous, Cornea and Iris with Ciliary Body After Subconjunctival Injection of 0.5 Cc of a Solution of Commercial Sodium Penicillin Containing 5,000 Oxford Units of Penicillin per Cubic Centimeter

	Concentration, Units/Gm or Cc					
	1 Hour		2 Hours		4 Hours	
	Cup Method	Dilution Method	Cup Method	Dilution Method	Cup Method	Dilution Method
Aqueous	0.68	1.0	1.04	1.6	0.5	
	0.8	0.8	1.14	0.4	0.51	
	1.4	1.0	0.7	0.5	0.2	
	0.82	0.8	0.63	0.5	0.26	
		0.75				0.2
		0.75				0.4
						0.2
Average	0.93	0.91	0.88	0.75	0.37	0.17
Cornea	75.5		30.6		Trace	
	61.4		57.5		Trace	
	43.1		23.7		Trace	
	32.8		27.8		Trace	
Average	53.2		34.9			
Iris with Ciliary Body	23.1		Trace		Trace	
	12.6		Trace		Trace	
	7.1		Trace		Trace	
Average	14.3					

ford units, with an average of 14.3 Oxford units, per gram wet weight The bulging of the conjunctiva was but little decreased two hours after injection and was still marked at the four hour interval The quantity of penicillin in the aqueous, 0.88 Oxford unit per cubic centimeter, was slightly less after two hours than after one hour No measurable amount of penicillin was detected in the vitreous fluid In the second hour after the injection the cornea lost 30 per cent of the penicillin present after the first hour At this time the iris with the ciliary body exhibited only traces of penicillin activity The decrease in the penicillin concentration in the examined fluids and tissues continued in the period that followed, only traces were found in the cornea after four hours and only 1 of 6 samples of aqueous contained a detectable amount of penicillin after six hours

Comment—A previous study on the penetration of alkaloids<sup>4</sup> into the eye showed that comparatively small quantities of salt solutions enter the aqueous after subconjunctival injection This observation appeared to be confirmed by the investigations of Struble and Bellows on subconjunctival injection of penicillin The concentrations in the aqueous and in the iris with the ciliary body in the present study were similar to those given by Struble and Bellows, but there was considerable difference in the amounts of penicillin determined in corneal extracts The diversity may be explained by variations in the technic—that is, in the placing of the depot, in the amount of the solvent and in the time of sampling The vitreous demonstrated a trace of penicillin activity in 1 instance and none in 5 instances, whereas Struble and Bellows reported the presence of 1.9 Oxford units per cubic centimeter of vitreous fluid The value of this figure is uncertain in view of the authors' statement, "Caution must be exercised in interpreting results since the number of experiments performed was small" From the present series of experiments on rabbits it can be concluded that the penicillin content of the cornea and the iris with the ciliary body is considerable, whereas the concentration in the aqueous is low and that in the vitreous negligible

The conspicuous bulging of the conjunctiva visible for four to six hours was apparently due to the accumulation of tissue fluid, since the concentration of penicillin in the aqueous and tissue extracts decreased steadily after the first hour There was no indication that any of the examined fluids and tissues retained penicillin for more than six hours

The solution of penicillin injected contained 5,000 Oxford units per cubic centimeter It is questionable whether solutions of this strength can be employed subconjunctivally in the human eye without producing a severe reaction In 2 patients a solution containing 2,000 Oxford units per cubic centimeter caused obvious discomfort

IONTOPHORESIS

Technic—Two solutions of commercial sodium penicillin containing 1,000 and 5,000 Oxford units per cubic centimeter, respectively, were prepared in a 0.9 per cent solution of sodium chloride The technic for iontophoresis was the same as that described in previous articles<sup>5</sup>, that is, a galvanic current of 2 milliamperes was applied from the cathode for five minutes with the

4 von Sallmann, L Iontophoretic Introduction of Atropine and Scopolamine into the Rabbit Eye, Arch Ophth 29 711 (May) 1943  
5 von Sallmann, L Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infection with Pneumococcus, Arch Ophth 30 426 (Oct) 1943

eye under local anesthesia using the corneal route. Determination of the penicillin activity of the ocular fluids and tissue extracts was carried out with the same technique as that described in the experiments with subconjunctival injection and was extended to the lens. After dissection, the lens was dipped in isotonic solution of sodium chloride to wash off adhering aqueous, it was then weighed, ground with quartz sand and diluted to four times its weight with buffer solution. In the series in which solutions containing 1,000 Oxford units per cubic centimeter were applied, the determinations were confined to a one hour interval. In the series with a solution of 5,000 Oxford units per cubic centimeter, determinations were made one, four, six and eight hours after iontophoresis.

**Results**—A single iontophoretic application of the solutions containing 1,000 to 5,000 Oxford

units meter the concentrations of penicillin in the aqueous were greatly increased (table 2). After one hour an average of 19.2 Oxford units per cubic centimeter was determined by the dilution method, the cup method gave considerably lower readings, with an average of 9.9 Oxford units per cubic centimeter. Possible explanations for the difference in the results with the two methods will be given later. In the cornea the concentration varied from 201.6 to 357.5 Oxford units per gram wet weight. The average concentration in the ciliary body was 65.9 Oxford units, with variations between 40.4 and 85.4 Oxford units per gram wet weight. The

TABLE 2—Concentration of Penicillin in the Aqueous, Cornea and Iris with Ciliary Body After Iontophoresis with a Solution of Commercial Sodium Penicillin Containing 5,000 Oxford Units of Penicillin per Cubic Centimeter

	Concentration, Units/Gm. or Cc.							
	1 Hour		4 Hours		6 Hours		8 Hours	
	Cup Method	Dilution Method	Cup Method	Dilution Method	Cup Method	Dilution Method	Cup Method	Dilution Method
Aqueous	11.84 9.12 8.68 10.52 9.44	19.2 19.2 19.2 19.2 19.2	3.44 1.8 1.9 3.5 1.7	2.4 3.25 3.25	0.48 0.40 0.44 0.33 0.41 0.44		0.17 0.19 0.67 0.13	
						0.44 0.1 0.375 0.5		— — —
Average	9.92	19.2	2.87	2.97	0.42	0.35	0.14	
Cornea	357.5 241.0 201.6		53.8 91.2 110.7 94.3 89.7		104.0 153.1 71.9 70.1 20.6 20.3		— Trace — —	
Average	266.7		88.3		73.3			
Iris with Ciliary Body	85.4 70.9 40.4		Trace Trace Trace 29.8 21.1		Trace Trace Trace — Trace		— — — —	
Average	65.9				—			

units per cubic centimeter did not cause damage of the corneal epithelium except for a transient haze. One hour after iontophoresis with a solution of 1,000 Oxford units per cubic centimeter, the average penicillin content of the aqueous for 6 experiments was 3.3 Oxford units per cubic centimeter as determined by the dilution method and 2.2 Oxford units as determined by the Oxford cup method. The average concentration of penicillin in the extract of the cornea was 103.5 Oxford units per gram wet weight. The extract of the iris with ciliary body had a concentration of 54.9 Oxford units per gram wet weight in 1 instance. In 4 instances the twentyfold dilutions contained only traces of penicillin. Neither the vitreous fluid nor the diluted lens extract showed any penicillin activity.

With the application of a solution of penicillin containing 5,000 Oxford units per cubic centi-

undiluted vitreous fluid and the lens tissue diluted four times its weight again did not contain measurable amounts of penicillin.

There was a continuous decrease in the concentration of penicillin in the aqueous within the seven hours following the first determination. The average of 2.97 Oxford units per cubic centimeter determined after four hours was approximately one sixth of the amount determined after one hour. At the eight hour interval an average of 0.14 Oxford unit per cubic centimeter was estimated. The depletion of the penicillin in the anterior part of the uvea was similar to that in the aqueous. The corneal extract contained after four hours about one third of that after one hour and slightly less after six hours. A steep decline in the concentration of penicillin in the cornea occurred after this time.



*Comment*—The preparation of penicillin employed in a previous study was found to cause considerable damage in a concentration of more than 2.5 mg per cubic centimeter<sup>3</sup>, the damage may have been due to the alcohol with which the free acid of penicillin was treated in the process of converting it to sodium penicillin. The commercial sodium salt was tolerated by the rabbit eye in an approximate concentration of 11 mg per cubic centimeter when a single iontophoretic application was given<sup>6</sup>. The same concentration was used in daily iontophoretic

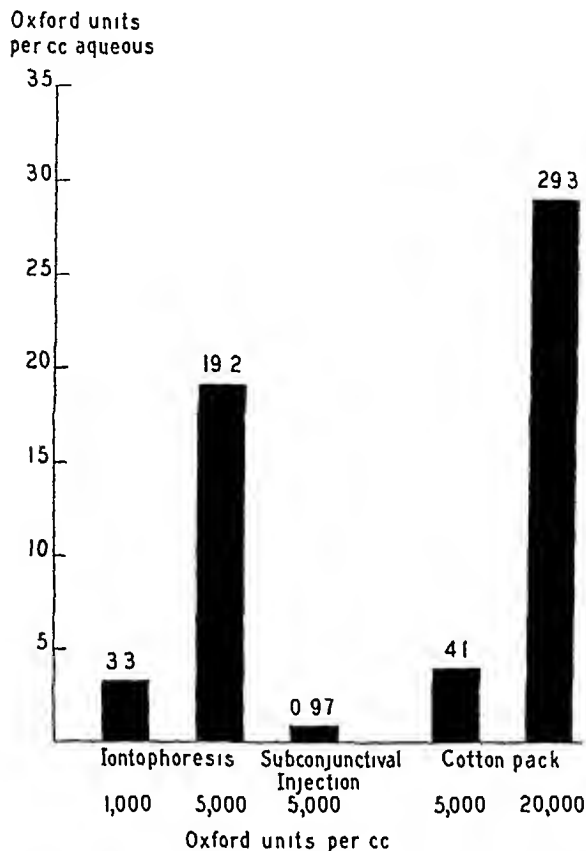
of one series, the sutures and cotton packs were removed after one hour. The globes were enucleated at the end of one, four and six hours, respectively, and were rinsed with saline solution to remove penicillin remaining on the surface. The subsequent technique was the same as that described in the experiments with subconjunctival injection. In one series the packs were removed and the eyes enucleated after two hours. All experiments were repeated three to nine times.

*Results*—One hour after the insertion of the cotton pack saturated with 0.1 cc of a solution containing 5,000 Oxford units per cubic centimeter, the part of the conjunctiva with which it had been in contact was moderately edematous, no other change was noticeable. The average concentration of penicillin in the aqueous after one hour was 4.1 Oxford units per cubic centimeter (figure). The amount of penicillin determined in the cornea ranged from 260.5 to 401.9 Oxford units, with an average of 347.2 Oxford units, per gram wet weight. The penicillin content of the iris with the ciliary body was also high, ranging from 69.9 to 100.6 Oxford units, with an average of 85.0 Oxford units, per gram wet weight.

When the packs were kept in the conjunctiva for two hours, a definite increase of penicillin activity was noted both in the aqueous and in the cornea, and the depletion in the iris with the ciliary body was almost complete. Undiluted vitreous fluid did not show antibacterial activity at the intervals tested. Determinations at longer intervals were not carried out.

Cotton packs saturated with 0.1 cc of a solution containing 20,000 Oxford units of penicillin per cubic centimeter were applied for one hour. The edema of the conjunctiva in these experiments was more pronounced than that described in the experiments with a solution containing 5,000 Oxford units per cubic centimeter. The conjunctiva, the subconjunctival tissue and the marginal area of the lower half of the cornea occasionally presented a yellow discoloration at the one hour period. In 2 instances there was a haziness of the lower segment of the cornea, probably due to slight displacement of the cotton pack. The amounts of penicillin determined at this time were excessive and far surpassed the readings obtained after various types of application with weaker solutions. As table 3 shows, the average concentration of penicillin in the aqueous was 29.3 Oxford units per cubic centimeter as determined by the dilution method and 23.7 Oxford units per cubic centimeter as determined by the Oxford cup method.

The corneal extract contained penicillin in such unexpectedly high concentrations that the dilutions in the first 4 experiments were not great enough to assure reliable readings. Later ex-



Concentration of penicillin in the aqueous one hour after various methods of local application

treatment of infections of the human eye without undue effect

#### APPLICATION OF COTTON PACKS SATURATED WITH SOLUTIONS OF PENICILLIN

*Technic*—Small pieces of absorbent cotton were soaked with 0.1 cc of a solution of sodium penicillin. Two concentrations, 5,000 and 20,000 Oxford units per cubic centimeter, were employed. The higher concentrations were selected in conformity with the work of Struble and Bellows,<sup>1a</sup> who instilled solutions of similar strength. Local anesthesia was used to increase the permeability of the cornea, and brief ether anesthesia was also employed to permit the insertion of two mattress sutures at the lid borders. After the saturated cotton packs were placed in the lower fornix of the conjunctiva, the sutures were tied. With the exception

<sup>6</sup> Higher concentrations were not used, in order to economize on the penicillin.

periments revealed an average of 1,728.9 Oxford units, with values from 1,107.7 to 2,535.2 Oxford units, per gram wet weight. The extracts of the iris with ciliary body also contained relatively large amounts of penicillin, ranging from 255.7 to 637.4 Oxford units, with an average of 465.1 Oxford units, per gram wet weight.

TABLE 3—Concentration of Penicillin in the Aqueous Cornea and Iris with Ciliary Body After Application of a Cotton Pack Saturated with a Solution of Commercial Sodium Penicillin Containing 20,000 Oxford Units of Penicillin per Cubic Centimeter

	Concentration, Units/Gm. or Cc					
	1 Hour		4 Hours		6 Hours	
	Cup Method	Dilution Method	Cup Method	Dilution Method	Cup Method	Dilution Method
Aqueous	28.4	30.6	4.8	2.4	0.52	0.5
	25.2	30.2	5.7	3.2	1.44	1.0
	9.0	8.9	0.55	0.6	0.5	0.25
	14.0	17.8	3.6	2.5	0.52	0.5
	30.2	40.0				
	35.2	40.0				
		24.0				
		24.0				
		48.0				
Average	23.7	29.3	3.7	2.2	0.75	0.56
Cornea	1,107.7		72.1		40.7	
	1,661.7		97.8		51.2	
	1,611.1		99.1		13.6	
	2,535.2				14.5	
Average	1,728.9		89.7		30.2	
Iris with Ciliary Body	63.74		31.5		Trace	
	479.3		50.4		Trace	
	628.4		66.7		Trace	
	414.6					
	451.1					
	254.7					
	255.7					
	599.4					
Average	465.1		49.9			

Despite the abundance of penicillin in various parts of the anterior segment, not more than a trace of it was found in the lens and none in the undiluted vitreous fluid. Four hours later the aqueous had an average concentration of 2.2 (dilution method) and 3.7 (Oxford cup method) Oxford units per cubic centimeter. The content of penicillin in the cornea dropped at this period to about one-twentieth, and that in the iris with the ciliary body to about one-tenth, the content after one hour. Traces of penicillin were again found in the diluted lens extract, but no penicillin was detected in the undiluted vitreous fluid. Depletion after six hours had advanced in the aqueous to an average of 0.56 (dilution method) and 0.75 (Oxford cup method) Oxford unit per cubic centimeter. The corneal extract was estimated to contain at this time approximately 30.2 Oxford units of penicillin per gram wet weight, and the diluted extract of the iris with the ciliary body showed only traces of penicillin.

*Comment*—Large quantities of penicillin were obtained in the aqueous, cornea and iris with ciliary body when determinations were made immediately after the removal of the packs (20,000 units per cubic centimeter) which had been in place for one hour. These readings greatly surpassed those of Struble and Bellows, who applied an excess of solution containing 20,000 Oxford units of penicillin per cubic centimeter in the conjunctival sac of the rabbit and clamped the lids for a period of thirty minutes to three hours. The highest concentrations which they tabulated were as follows: aqueous, 15 Oxford units per cubic centimeter; cornea, 45 Oxford units per gram wet weight, and iris with ciliary body, 35 Oxford units per gram wet weight. Despite the high initial values achieved with the insertion of the packs, the depletion of penicillin was almost complete after six hours, as table 3 shows.

#### COMMENT ON EXPERIMENTAL INVESTIGATION

When a solution of penicillin containing 5,000 Oxford units per cubic centimeter was applied, the iontophoretic administration resulted in the highest concentrations of penicillin in the aqueous fluid (figure). This amount of penicillin was obtained one hour after ionization for five minutes whereas after subconjunctival injection and the insertion of the cotton pack the depots of penicillin remained in place for one hour. The cornea and the iris with ciliary body contained more penicillin after application of the pack. Although a dilution of the administered penicillin of course occurred, the subconjunctival fluid as well as the cotton pack were still yellow at the one hour interval.

The highest penicillin levels by far were observed after the cotton packs saturated with a solution containing 20,000 Oxford units per cubic centimeter were applied for one hour. The aqueous contained approximately 50 per cent more penicillin than after iontophoresis with a solution of penicillin having 5,000 Oxford units per cubic centimeter, and the cornea and iris with ciliary body contained five to eight times as much.

None of the methods of topical application secured more than traces of penicillin in the vitreous fluid and the lens. This observation strongly suggests that neither iontophoresis

7 Neely, J. C., and Cross, A. G. Penicillin Lamellae in Eye Conditions, *Lancet* 1:85 (Jan 20) 1945. These authors suggested the use of lamellae containing penicillin in the eye. The results of studies on the penetration of penicillin into the eye from lamellae have not been reported.

through the cornea nor the administration of cotton packs nor subconjunctival injection will be effective in treatment of deep infections of the lens or vitreous. After a single iontophoretic application with a solution of penicillin containing 5 000 Oxford units per cubic centimeter a bacteriostatic level of penicillin remained in the aqueous over a period of eight hours. The gradient of depletion was steeper in the experiments with cotton packs saturated with a solution containing 20,000 Oxford units per cubic centimeter so that the concentration in the aqueous after four hours was approximately the same as that following iontophoresis with a solution containing 5 000 Oxford units per cubic centimeter at the same interval.

The individual values within the single series of experiments were at considerable variance. Anatomic differences in rabbits' eyes and unavoidable inaccuracies in the technic of application may explain in part the diversity of the results. Also relatively inexact are the bioassay methods applied. In addition, the extraction and processing of the tissue fluids increase the limits of error far beyond those estimated by Florey for the cup method. This does not explain, however, the differences in several series in which the two types of penicillin determinations were made on the same sample of aqueous fluid. The divergence was most striking in the series in which a solution containing 5,000 Oxford units per cubic centimeter was applied iontophoretically (table 2, columns 1 and 2). The measurements with the Oxford cup method were taken at the upper end of the standard curve and are, therefore, less reliable than those obtained with the dilution method. Another explanation is suggested by the experiments of Chow and McKee,<sup>8</sup> who showed that penicillin combined with serum albumin to form a penicillin-albumin complex that possessed antibiotic activity. It is possible that the formation of such a complex in the aqueous which is rich in protein after iontophoresis interfered with the diffusion of the sample in the cup method. More experiments are planned, however, to demonstrate whether this factor accounts for the divergence of the comparable figures secured by the two methods of determination after iontophoresis.

#### PENETRATION OF PENICILLIN INTO THE AQUEOUS OF HUMAN EYES

Studies on the penetration of sulfonamide drugs into the eye have demonstrated that the

results derived from experiments on laboratory animals especially rabbits, can be applied to the human eye only with caution. Rabbit experiments were the basis for all of the present and previous investigations carried on in this laboratory, most of those of Bellows and Struble and those of Leopold and LaMotte concerning the penetration of penicillin into the eye. It was advisable, therefore, to estimate the amount of penicillin in the aqueous of suitable human eyes after topical administration. The examinations of aqueous were carried out on eyes which were to be enucleated. Instillations and application of cotton packs were selected as being least disturbing to the patient.

*Technic*—After local anesthesia with tetracaine, 4 drops of a solution of commercial sodium penicillin containing 20,000 Oxford units of penicillin per cubic centimeter was instilled in 1 instance, and cotton packs saturated with 0.1 cc of a solution of penicillin of the same strength were placed in the lower fornix in 3 instances. The eyes were patched until the withdrawal of the aqueous one to two hours later. The aqueous was appropriately diluted with phosphate buffer, and the penicillin content was determined by the Oxford method.

*Results*—The following observations were made.

CASE 1—L. N., aged 46, had a lesion diagnosed as a small circumscribed malignant melanoma above the disk. The anterior segment of the eye was normal. One and one-half hours after the insertion of the cotton pack the aqueous was estimated to contain 2.3 Oxford units of penicillin per cubic centimeter.

CASE 2—M. S., aged 50, had a lesion diagnosed as a small malignant melanoma near the optic nerve. The anterior segment was normal. One hour after the insertion of the cotton pack no penicillin was detected in a fourfold dilution of the aqueous.

CASE 3—A. G., aged 74, had a condition diagnosed as absolute glaucoma. A flat scar was present in the limbus after an Elliot operation (1934). The globe showed marked circumcorneal injection and was hard (tension plus 3). The cornea was slightly hazy and the anterior chamber shallow. One hour and fifteen minutes after insertion of the cotton pack, the aqueous was estimated to contain approximately 9 Oxford units of penicillin per cubic centimeter.

CASE 4—F. O., aged 17, had a condition diagnosed as endophthalmitis following a perforating injury with an intraocular foreign body near the posterior pole of the globe. The eye showed intensive mixed injection, a cloudy cornea and a swollen and hyperemic iris. Two hours after the instillation of penicillin, the aqueous was estimated to contain approximately 0.6 Oxford unit of penicillin per cubic centimeter.

*Comment*—Two observations on aqueous fluid from human eyes with normal anterior segments indicated that the values were more erratic than those secured in normal rabbit eyes. The average amount of penicillin in the aqueous was approximately one twentieth of that determined in rabbits. The negative result in case 2

<sup>8</sup> Chow, B. F., and McKee, C. M. Crystalline Penicillin and Human Plasma Proteins. *Science* **101**: 67 (Jan 19) 1945.

may have been caused by the reflex tearing due to the mechanical irritation

The pathologic condition of the cornea probably explains the relatively high concentration of penicillin in the aqueous of the glaucomatous eye (case 3). The single instillation of 4 drops of a solution of penicillin containing 20 000 Oxford units per cubic centimeter, however, produced in the inflamed eye in case 4 a concentration of penicillin which was only about one-fifth that found by Bellows and Struble in the normal rabbit eye with the same technic. It is not feasible, therefore, to apply directly to the human eye the values tabulated by Leopold and LaMotte for the aqueous of rabbits with abraded or inflamed corneas and to conclude that instillations or the application of ointments can be substituted for iontophoresis or other vigorous procedures in the treatment of intraocular infections.

On the basis of *in vitro* experiments, the question arises again whether the attempts to increase the concentration of penicillin in eyes with intraocular infections are justified. Garrod<sup>9</sup> observed that the relatively impure commercial penicillin tested against *Staphylococcus aureus* was less active in high concentration than in low. He stated

The only good reason for using strong solutions in local treatment is to ensure that loss by escape, dilution, or absorption shall not permit the concentration to fall below the minimum level for full effect

The data presented in this paper indicate that the conditions requiring the use of concentrated solutions exist in treatment of intraocular infections. If the initial level of the drug substantially exceeds the effective concentration, the presence of the minimal effective amount will be prolonged so that the deeper foci are more likely to be beneficially influenced. It should be stressed that the ratio between the concentration of the solution administered and the concentration of the drug determined in the aqueous was about 260:1 to 300:1 after use of the ionization method and about 660:1 to 1,200:1 after employment of the pack technic. Further-

more, it was apparent from a small number of studies that this ratio became even more unfavorable in the human eye. There is, therefore, a sound theoretic basis for preferring vigorous procedures in treating exogenous infections of the anterior segment of the human eye.

#### SUMMARY

1. A comparison of the results of subconjunctival injection, iontophoresis and application of cotton packs using a solution of commercial sodium penicillin containing 5,000 units of penicillin per cubic centimeter, showed that the highest concentration was obtained in the aqueous by iontophoresis and in the cornea and the iris with ciliary body by the prolonged application of cotton packs. The lowest concentration of penicillin in the aqueous, the cornea and the iris with ciliary body was observed after subconjunctival injection.

2. Extremely high concentrations of penicillin were determined in the cornea and the iris with ciliary body after the application of cotton packs saturated with a solution of sodium penicillin containing 20 000 Oxford units of penicillin per cubic centimeter. The penicillin content of the aqueous was also higher than that obtained with the other methods tested.

3. The depletion of penicillin from the ocular tissues and the aqueous was almost complete eight hours after iontophoresis with a solution of sodium penicillin containing 5,000 Oxford units of penicillin per cubic centimeter and after application of cotton packs saturated with a solution containing 20,000 Oxford units per cubic centimeter.

4. In general, not more than traces of penicillin were demonstrated in either the lens or the vitreous after topical administration.

5. Determinations on human eyes with normal and with edematous corneas gave more erratic results and much lower values than determinations on rabbits' eyes.

Dr. John H. Dunnington, Dr. Raymond Pfeiffer and Dr. Thomas Johnson permitted the report of their cases.

Miss Jeanette Di Grandi and Miss Mary Glyde Marsh gave technical assistance.

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<sup>9</sup> Garrod, L. P. Action of Penicillin on Bacteria, *Brit. M. J.* 1: 107 (Jan. 27) 1945.

# VITAMIN C SATURATION AND SENILE CATARACT

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Vitamin C ( $C_6H_8O_6$ ) is readily soluble in water and alcohol and insoluble in ether and benzene and has a molecular weight of 176. Fehling's solution is reduced in cold by vitamin C, as is silver nitrate, permanganate and iodide. Von Szent-Gyorgyi produced vitamin C in 1932 and named it hexuronic acid, without being aware of its true identity. The final identification was made by Tillmans. Vitamin C is characterized by a high redox potential, which is strongly negative. The reduced form of vitamin C activates ferments and inactivates the oxidized form of the same. This vitamin is readily destroyed by oxidation and is a strong reducing agent in itself. Important organs containing ascorbic acid are the adrenals, the lens, the corpus luteum, the brain, the hypophysis, the pancreas, the aqueous and, in lesser amounts, the vitreous. In the blood 8 to 12 mg per thousand cubic centimeters represents the normal average.

Investigators are unanimous in the opinion that the amount of vitamin C present in the lens and in the aqueous is much higher than in other tissues or in the blood. However, there is a wide discrepancy in the explanations of how this high concentration of vitamin C is produced. This increased amount can be derived either from the blood or through synthesis by the lens. The origin of vitamin C in the lens must still be considered an unsolved problem. It may be that the sugar present in the lens is converted by dehydration into ascorbic acid during glycolysis, with the cystine-cysteine group serving as a hydrogen acceptor, but the conversion might also be due to the reaction of sugar and oxidized glutathione, yielding ascorbic acid and reduced glutathione. It has been proved that in the aging and clouded lens the cysteine group tends to disappear and the cataractous lens is composed of water-soluble and cysteine-free albuminoid. Vitamin C behaves analogously, diminishes as the lens becomes progressively opaque and disappears when the opacification is complete. Since the vitamin C content of the normal aqueous is much higher than that of the blood

and since some authors believe this relation is not present in the aphakic eye, the place of origin would seem to be in the lens.

Normal transparency of the lens is linked with normal metabolism. The foundation of the latter is oxidation, the mobilization of hydrogen and the activation of oxygen by help of oxidative ferments. Breathing of the lens is the most important form of oxidation, and in this process the presence of catalyzers, responsible for the oxidation-reduction system, is of paramount significance.

The lens, being devoid of a blood supply, is especially dependent for its normal metabolism on intracellular substances which form oxidation-reduction systems. Birch and Dann<sup>1</sup> were the first to describe the presence of large amounts of vitamin C in the lens of sheep. According to Glick and Biskind,<sup>2</sup> no apparent significance could be attached to the concentration of vitamin C in the lens with regard to the capacity of some animals (such as the rat, rabbit, sheep, ox, cow and horse) to synthesize vitamin C and the lack of this capacity in animals such as the guinea pig and man, who must derive vitamin C from their food. Variations in the concentrations of vitamin C in the lens between these two groups is less than the variations within each group. Thus, the very low value for the rat lens stands in striking contrast to the much higher values for the lenses of other animals of the group capable of synthesizing the vitamin. Muller<sup>3</sup> established high values for the aqueous and the lens of man and animals and considered the possibility that the lens forms vitamin C from sugar. Aging and cataract formation result in diminished sugar and vitamin C contents.

1 Birch, T W, and Dann, W J. Ascorbic Acid in the Eye-Lens and Aqueous Humor of the Ox, *Biochem J* **28** 638, 1934, Estimation and Distribution of Ascorbic Acid and Glutathione in Animal Tissues, *Nature* London **131** 469, 1933.

2 Glick, D, and Biskind, G R. Studies in Histochemistry. Distribution of Vitamin C in Lens of Eye, *Arch Ophth* **16** 990 (Dec) 1936.

3 Muller, H K. (a) Zur Kenntnis der durch Naphthalin hervorgerufenen biochemischen Augenveränderungen und ihre Beeinflussung durch Vitamin C, *Arch f Augenh* **109** 304, 1935, (b) C-Hypovitaminose und Altersstar, *Klin Monatsbl f Augenh* **100** 478, 1938.

of the lens, according to Fischer's hypothesis, the production follows the already mentioned formula: sugar + oxidized glutathione = vitamin C + reduced glutathione. The experiments of Guha and Ghosh demonstrated the production of vitamin C by enzymatic synthesis through the tissues, especially liver *in vitro*, and the striking faculty of the lenses of young animals to produce ascorbic acid through synthesis.

The important observation that the vitamin C content of the normal lens diminishes in proportion to the formation of cataract to values approaching zero and, furthermore, that aging of the lens similarly results in decrease of the vitamin C content seems to substantiate the belief that vitamin C is of extreme importance for the respiration of lens tissue. The high vitamin C concentration in the aqueous as compared with that in the blood can be explained on the assumption that the vitamin C content of the aqueous is derived either from the blood or from the lens. Increased intake of vitamin C results in greater excretion in the urine without an increase in the blood level or in the concentration in the aqueous, thus revealing elective filtration rather than ultrafiltration. Von Euler and Malmberg<sup>4</sup> claimed that the antiscorbutic action of the lens is based on the presence of vitamin C, which is much more marked in young animals, thus corroborating the statement that the aging organism and all its structures are poorer in vitamin C and confirming the observation that the amount of the vitamin is lessened in cataractous lenses.

Muller gave the vitamin content of the normal aqueous as 12.8 per hundred cubic centimeters. Nakamura and Nakamura<sup>5</sup> found similarly high concentrations, but for patients with cataractous lenses they obtained a value of 2 to 8 mg per hundred cubic centimeters and for patients with complicated cataracts, a value of 0.5 mg per hundred cubic centimeters, thus showing a striking decrease in the aqueous of the aged and of persons with cataract. They observed decreased concentrations in the lens itself, especially in the nucleus. The nucleus has a smaller amount of vitamin C, even in the transparent lens (Glick and Biskind).

Nordmann reported a decrease of ascorbic acid in the cataractous lens to 0.0026 mg per hundred grams of tissue (the normal was given as from 0.011 to 0.016 mg per hundred grams).

4 von Euler, H. V., and Malmberg, M. Neue Versuche "ueber Ascorbinsaure (C-Vitamin) in tierischen Augenlinsen, *Arch f Augenh* **109** 225, 1935.

5 Nakamura, B., and Nakamura, O. Ueber das Vitamin C in der Linse und dem Kammerwasser der menschlichen Katarakte, *Arch f Ophth* **134** 197, 1935.

Urbanek<sup>6</sup> derived a change in the vitamin C content of from 1.95 to 14 mg per hundred cubic centimeters in the aqueous and of from 0.003 to 0.40 mg per hundred grams in the lens. Hawley and Pearson<sup>7</sup> found a decreased vitamin C content of the cataractous lens and ventured the opinion that the decreased amount of food is responsible for the decrease in the tissues of aging persons and that the decrease within the cataractous lens is only secondary.

A decrease of vitamin C concentration in the aqueous and in the lens of persons with cataract seems to be well established, in the blood the maximum level for such persons is cited as corresponding to the minimum level for normal persons. There is seemingly some connection between the vitamin C level of the blood and the formation of lenticular opacities, a relation which suggests hypovitaminosis C of the lens affected. Hawley and Pearson<sup>7</sup> reported low blood levels in persons with cataract. Bellows<sup>8</sup> found for normal persons 1.02 mg and for cataractous persons (20 cases) only 0.05 mg per hundred cubic centimeters, the findings of Urbanek,<sup>6</sup> Gapeev<sup>9</sup> and others represent similarly low values for cataractous patients. According to Bellows, the low level of ascorbic acid in the blood is instrumental in producing the decreased amount in the aqueous, a circumstance predisposing to formation of opacities within the lens. In Muller's opinion, cataract is the result of disturbed metabolism of the lens accompanied with changes in the chemical composition due to decrease of ascorbic acid. Many authors believe that the source of vitamin C in the aqueous lies in the blood, normal aqueous contains the vitamin only in the reduced form and in a concentration not corresponding to that of the blood. According to Goldmann and Buschke,<sup>10</sup> the high concentration of vitamin C in the aqueous is partly the product of the metabolism of the lens. The lens is capable of reducing the oxidized form derived from the blood, a fact partially

6 Urbanek, J. Der C-Vitamin-Stoffwechsel bei Starkkranken, *Klin Monatsbl f Augenh* **101** 670, 1938.  
Urbanek, J., and Albrecht, W. C-Vitamin und Lebensalter, *Ztschr f Augenh* **95**, 192, 1938.

7 Hawley, E., and Pearson, O. Vitamin C and Its Relation to Cataract, *Arch Ophth* **19** 959, (June) 1938.

8 Bellows, J. Biochemistry of Lens. Cevitamic Acid Content of the Blood and Urine of Subjects with Senile Cataract, *Arch Ophth* **15** 78 (Jan) 1936.

9 Gapeev, P. I. Ascorbic Acid Content of Aqueous Humor, Crystalline Lens and Blood in Cataract Patients and in Normal Persons, *Vestnik oftal* **18** 154, 1941.

10 Goldmann, H., and Buschke, W. Blutkammerwasserschranke und Vitamin C, *Arch f Augenh* **109** 205 and 314, 1935, Berichtigung und Nachtrag zu der Arbeit Blutkammerwasserschranke und Vitamin C, *ibid* **109** 689, 1936.



explaining the amount of reduced vitamin C in the aqueous, but, as emphasized by Muller, only a small portion of the vitamin in the aqueous is the product of the lens. The concentration of vitamin C in the aqueous is ten times that in the blood and represents both the oxidized and the reduced phase. Subconjunctival injections of hypertonic saline solution or intravenous injections of theophylline lead to a decrease of ascorbic acid in the aqueous, owing to increased permeability of the blood-aqueous barrier, the complicated cataract due to prolonged inflammation, resulting in decrease in vitamin C concentration, is the clinical analogy to this mechanism. In Buschke's<sup>11</sup> opinion, the vitamin C content of the aqueous depends on the concentration in the blood of the reversible, oxidized, form of vitamin C, the oxidized form in the anterior chamber undergoes reduction through the action of the lens to the reduced phase of the redox system, the lens being the regulating mechanism of the redox potential. Similarly Monjukowa and Fradkin<sup>12</sup> stated the belief that the vitamin C of the aqueous derives from the blood through the elective function of the ciliary epithelium and unilateral permeability of the blood-aqueous barrier, the change in the latter in cataractous eyes produces the decrease of ascorbic acid. Weinstein's<sup>13</sup> examination disclosed the disappearance of cysteine and vitamin C in cataractous lenses, but in the capsule both were present. In his opinion, the sclerosis of the vessels of aging persons leads to decrease of vitamin C. In the production of the reduced form of vitamin C the lens liberates hydrogen and this form passes only with difficulty the blood-aqueous barrier. Muller's findings of loss of sugar and increase in ascorbic acid in the lenses of young animals and the reversed condition in older animals seem to be further substantiation of the vitamin C-producing mechanism of the lens. Monjukowa and Fradkin<sup>12</sup> found 20 mg per hundred grams in contrast to the concentration in other body tissues. Aging causes decrease, and in accordance with the slower metabolism of the nucleus the central portion is poorer than the cortical parts. Muller<sup>3</sup> and his co-workers reported that they had produced naphthalene cataracts in rabbits, and though there was no change in the concentration

of vitamin C in the lenses at first the values fell to as low as zero as they became cloudier. These cataracts could be prevented by feeding cabbage to the experimental animals, according to Bourne,<sup>14</sup> but Muller and Buschke<sup>15</sup> obtained inconclusive results through treatment of naphthalene cataracts with ascorbic acid. The relatively high concentration of vitamin C in the aqueous was confirmed by Gala and Mělka<sup>16</sup> who agreed that it must be the result of the lens mechanism, even though their results were lower than the value of 12.8 mg per hundred cubic centimeters obtained by Muller and Buschke. Tatsumi, Nagao, Okamura and Gamo<sup>17</sup> reported a notable increase of vitamin C in the aqueous after intravenous administration of ascorbic acid (and no change in the level in the spinal fluid), confirming the observation of Goldmann and Buschke<sup>10</sup> of a marked increase in the concentration in the aqueous, lasting several hours and the similar reports of Bietti<sup>18</sup> and Carteni. The aqueous of aphakic eyes has a much lower concentration of vitamin C (Muller and Buschke), showing that the lens protects vitamin C from oxidation by liberating hydrogen.

In the opinion of some authors, the decreased vitamin C of the aqueous is responsible for the formation of opacities in the lens, however, other investigators, such as Nordmann, Bietti and Carteni, did not accept the decrease as the direct cause of the opacities but regarded it only as a symptom of the metabolic disturbance of the lens.

In a recent paper Huysmans and Fischer<sup>19</sup> reviewed the various hypotheses offered to explain the increased concentration of vitamin C in the contents of the anterior chamber, the increased activity of the lens (Muller, Fischer) the reciprocal permeability of the blood-aqueous fluid partition for oxidized vitamin C

14 Bourne, M. C. Effect of Diet on Nature of Ocular Lesions Produced by Naphthalene, *Brit J Ophth* **17** 210, 1933.

15 Muller, H. K., and Buschke, W. Ueber die Behandlung der Naphthalinkatarakt mit Vitamin C, *Arch f Augenh* **108** 597, 1934.

16 Gala, A., and Mělka, J. Der Gehalt an Vitamin C im Humor aqueous des normalen und pathologisch veränderten Auges, *Arch f Augenh* **109** 726, 1936.

17 Tatsumi, M., Nagao, Y., Okamura, K., and Gamo, J. Ueber den Uebergang von Vitamin C in den Liquor und das Augenkammerwasser, *Klin Wchnschr* **14** 1007, 1935.

18 Bietti, G. B. Ulteriori ricerche intorno all'azione sul cristallino di regimi carenzati di vitamina e di cistina, *Boll d ocul* **14** 3, 1935.

19 Huysmans, J. H. B. M., and Fischer, F. P. Ueber die Ursachen der hohen Vitamin-C-Konzentration von Kammerwasser und Linse, *Ophthalmologica* **103** 21, 1942.

11 Buschke, W. Blutzirkulation im Auge und Vitamin C, *Arch f Augenh* **109** 691, 1936.

12 Monjukowa, N. K., and Fradkin, M. J. Neue experimentelle Befunde über die Pathogenese der Katarakt, *Arch f Ophth* **133** 328, 1935.

13 Weinstein, P. Bedeutung des C-Vitamins bei den biologischen Oxydationsvorgängen der Linse, *Arch f Augenh* **109** 221, 1935.

(Goldmann and Buschke<sup>10</sup>), the combined origin from the blood and lens (Podesta and Baucke<sup>20</sup>) and the stimulation of the epithelium through the parasympathetic system (Bonsignore)

According to Muller, the oxidized form of vitamin C appears in the aqueous through diffusion from the blood and becomes changed into the reduced form through activity of the lens. Fischer's concept of the production of vitamin C from carbohydrates through the metabolism of the lens as mentioned before represents a reversible oxidation-reduction system. 1 molecule of dextrose combining with 2 molecules of oxidized glutathione, resulting in 1 molecule of vitamin C and 4 molecules of reduced glutathione. Goldmann and Buschke stated the opinion that vitamin C exists in the blood in oxidized form. Subconjunctival injections of saline solution and intravenous administration of theophylline resulting in lessening of the amount present in the aqueous and injection of epinephrine not causing any increase in the concentration in the aqueous. Injection of vitamin C resulted after half an hour in the absence of the reduced form of vitamin C in the blood and a slight increase of the oxidized form but in a long-lasting increase in the concentration of the aqueous. Increased concentration in the blood was accompanied with increased concentration in the anterior chamber. According to Fischer vitamin C in the blood almost always exists as the reduced form, and the decreased concentration following injection of epinephrine is due to oxidation of vitamin C and not to rendering impermeable the blood-aqueous partition, accordingly, substitution of epinephrine by atropine produces an increased concentration of vitamin C in the aqueous. Furthermore, the concentration of vitamin C in the aqueous of the aphakic eye approaches that of the blood, in certain types of secondary cataract the presence of newly formed lens tissue is responsible for the increased amount of ascorbic acid present.

The lens not only produces vitamin C but reduces large quantities of the oxidized form. The concentrations of vitamin C in the lens and aqueous regulate the transparency of the lens, the concentration may be normal in lenses with nuclear sclerosis with functioning clear cortical parts. The circulation of the aqueous toward and the return circulation from the lens and the circulation within the lens itself are the factors representing the reduction of vitamin C.

20 Podesta, H., and Baucke, J. Woher kommt das Vitamin C in den verschiedenen Geweben des Auges? Herkunft aus dem Blute und Synthese in der Linse, *Arch f Ophth* **139** 720, 1938

The hypothesis of Fischer concerning the concentration of the vitamin in the aqueous of aphakic eyes is seemingly contradicted by many authors. Urbanek reported a wide variation of the concentration in aphakic eyes, which apparently is in contradiction to the concept that the lens is responsible either for the amount or for the production of vitamin C in the aqueous. Franta<sup>21</sup> found that the aqueous of young aphakic persons years after the operation contains various amounts of vitamin C, values which approach the level for eyes without aphakia. For an 11 year old child, nine years after the operation the concentrations for the two eyes were 14.80 and 11.28 mg per hundred cubic centimeters, respectively, for a 7 year old child two years after the operation, the value was 6.52 mg, and, finally for a 5 year old child, six months after the operation the concentrations were 3.52 and 4.23 mg per hundred cubic centimeters. Bakker,<sup>22</sup> on the other hand, reported decreased concentrations in cases of aphakia. The possible role of vitamin C in the metabolism of the lens and the relation of its disturbance to formation of cataract led the investigations in the direction of a systemic disturbance of the vitamin C metabolism in patients with senile cataract. It is clear that the patients with cataract do not show clinical symptoms of hypovitaminosis C. Mild deficiency may cause weakness, headache, restlessness, tenderness of the joints, retarded growth, impaired digestion, defective teeth, lowered resistance to infection and slow union of fractures. Pronounced deficiency may cause scurvy, characterized by capillary hemorrhages, epistaxis, swollen joints, gingivitis, loosened teeth, spontaneous fractures, anemia, muscle atrophy, infections of the respiratory and intestinal tracts, bloody diarrhea and hematuria, with death due to secondary infection or shock. Bakker emphasized that there are cases of complete lack of vitamin C in which the lenses are transparent. Scurvy is known never to cause cataract formation, nor does it occur in experimental animals in which the lens and aqueous have been depleted of vitamin C. In the experiments of Monjukowa and Fradkin it was produced only in the extreme stages, in which numerous factors besides the depletion of vitamin C could be blamed. This fact did not escape the attention of Williamson-Noble.<sup>23</sup>

21 Franta, J. L'acide ascorbique dans l'humeur aqueuse, *Compt rend Soc de biol* **126** 110, 1937

22 Bakker, A. Ueber die Bedeutung der Ascorbinsäure (Vitamin C) für den Stoffwechsel der Linse, *Arch f Ophth* **136** 166, 1936

but, in his opinion, it may be that ascorbic acid provides a method of lens respiration which serves as an alternative to that given by glutathione. When the latter mechanism is upset, as in the case of naphthalene or galactose cataract, vitamin C comes into its own, in fact, administration of the latter substance has been shown to delay the onset of galactose cataract, though not to the same extent as the use of cysteine, the amino acid-forming glutathione.

Research on the true role of vitamin C in cataract formation had to be extended, and studies concerned with the clinical and laboratory examinations of cataractous patients formed the next logical step in clearing up the question.

In normal, healthy persons the blood serum or plasma level and the urinary excretion of vitamin C are dependent on the dietary intake and the utilization of food. Normal adults, according to van Eekelen<sup>24</sup> and Heinemann,<sup>25</sup> have a daily requirement of the vitamin of 60 mg. The presence of infection is known to increase the requirement, the blood level of vitamin C in patients with infection may be reduced to the level found in patients with scurvy, and the amount of vitamin required to raise the blood plasma level to the value for the renal threshold and to maintain this degree of saturation is many times that accepted as a normal physiologic requirement. Similarly, patients with rheumatoid arthritis exhibit an apparent vitamin C deficiency.

By saturation is meant a state of supply of ascorbic acid such that after an increased intake 60 to 80 per cent of the additional vitamin will be excreted in the urine within eight to twenty-four hours. Hence, unsaturation exists when only a slight increase in excretion follows the added intake. This does not indicate that undersaturation is an abnormal state or that a supply inadequate to provide saturation will cause vitamin C deficiency. The majority of persons who do not show any detectable signs of deficiency are not saturated. The normal plasma level of 1.2 mg per hundred cubic centimeters falls in cases of scurvy to 0.2 mg per hundred cubic centimeters, but abnormally low levels are encountered without evidence of deficiency. The urinary excretion normally varies

from 10 to 30 mg daily. The amount varies not only with the method of analysis but with the protein content and the acid-base properties of the diet. Excretions above 15 mg of vitamin C daily suggest the absence of any deficiency, but persons excreting that amount may be saturated or may be very far from saturation. The requirements of aging bring with it the necessity for a larger amount of vitamin C. This statement seems to contradict the well known fact that advancing age requires less nutrition, on the other hand, the progressive atrophy of the organs makes the utilization of food more difficult. The absorption of dextrose in the intestine requires vitamin C. Therefore in the aged a higher requirement of vitamin C is probable for the proper upkeep of nutritional balance. Furthermore, in senescence the saturation suffers, owing to poorer absorption, facilitated by the often present suboptimal secretion of hydrochloric acid in the stomach and unsatisfactory mastication. All these circumstances may be instrumental in producing comparatively lower plasma levels, a decrease which is not necessarily indicative of vitamin deficiency. The plasma and blood levels and the urinary excretion do not give as accurate information concerning vitamin C nutrition as the saturation test—the measuring of urinary output following an added intake of the vitamin. Oral administration gives less accurate information than the intravenous method, with the former there are large factors of error due to variability of absorption and utilization from the gastrointestinal tract. Wright, Lilienfeld and MacLenathen<sup>26</sup> proposed a five hour test following intravenous injection. In our examinations the method of Finkle<sup>27</sup> was followed.

On the day of the test the patient was permitted the usual meals, with the exception of citrus fruit and other foods rich in vitamin C. There was no restriction of fluids. The urine was collected at 8 a. m. and at 10 a. m. and the vitamin C content determined for each specimen. After the 10 a. m. voiding 100 mg of ascorbic acid, dissolved in 5 cc of distilled water, was administered intravenously. The subject was requested to void at 12 30, 2 30 and 4 30 p. m., and the vitamin C content of each specimen was again determined. For the titration of ascorbic acid, 2,6-dichlorophenolindophenol, as used by Harris, Ray and Ward,<sup>28</sup> was employed. The injection in 220 aged subjects did not result in any untoward symptoms.

23 Williamson-Noble, F. A. Discussion of Role of Vitamins in Ophthalmology, *Tr Ophth Soc U Kingdom* (1942) **62** 53, 1943.

24 van Eekelen, M. On the Amount of Ascorbic Acid in the Blood and Urine. Daily Human Requirements for Ascorbic Acid, *Biochem J* **30** 2291, 1936.

25 Heinemann, M. On the Relation Between Diet and Urinary Output of Thiosulfate and Ascorbic Acid. Human Requirements for Vitamin C, *Biochem J* **30** 2299, 1936.

26 Wright, I. S., Lilienfeld, A., and MacLenathen, E. Determination of Vitamin C Saturation. Five Hour Test After Intravenous Test Dose, *Arch Int Med* **60** 264 (Aug) 1937.

27 Finkle, P. Vitamin C Saturation Levels in the Body in Normal Subjects and in Various Pathological Conditions, *J Clin Investigation* **16** 587, 1937.

28 Harris, L. J., Ray, S. N., and Ward, A. The Excretion of Vitamin C in Human Urine and Its Dependence on the Dietary Intake, *Biochem J* **27** 2011, 1933.

In the unselected series were included 200 patients with senile cataract, the ages varying from 50 to 84, and 20 patients with glaucoma without cataract, representing approximately the same age group. All patients were admitted for the purpose of surgical intervention, and the tests were made on the first day of hospitalization. Patients who refused the intravenous administration or did not cooperate in observation of the voiding time were necessarily excluded from the study.

The vitamin C output within twenty-four hours was usually about 13 to 20 mg, and the average excretion was between 0.03 and 0.05 mg per cubic centimeter of urine during the day and a somewhat lower amount during the night. The intravenous injection in normal subjects produces an increased excretion of about six times the preinjection amount, this means that, in addition to the usual daily excretion, 30 to 50 per cent (or more) of the injected amount is eliminated through the kidneys. For determination of the vitamin C saturation of the body, measurement of the excretion for eight hours, including the six hours following the injection, suffices. This procedure is highly satisfactory except in cases of impairment of renal function, in which delay in excretion may occur (Ludden and Wright<sup>29</sup>).

Of the 20 control subjects, 12 showed after the intravenous injection an excretion of from four to eight times the previous amount, and 5 patients, an excretion of from two to four times the preinjection value, in the remaining 3 subjects the urinary excretion was less than twice the preinjection value.

The distribution of values for the 200 unselected patients with cataract was as follows:

1 In 10 patients the excretion of vitamin C was increased to from six to eight times the amount preceding intravenous administration of ascorbic acid.

2 In 125 patients the urinary output was four to six times that established before the administration of ascorbic acid.

3 In 37 patients the output averaged only two to four times the preinjection value.

4 The remaining 33 patients showed less than twice the amount of vitamin C excreted before administration of the ascorbic acid.

When the ages of the patients are considered in relation to the vitamin C excretion in the urine, it is evident that the majority of the

patients with a high vitamin C excretion belonged to the lower age group (50 to 60 years) and, conversely, that the majority of the group with poor vitamin C saturation belonged to the higher age group (60 to 70 years and over 70 years).

The great majority of my patients (135) showed an excretion level approximating that found in the normal subjects living on an adequate mixed diet, a large percentage were within the age group of 50 to 60 years. In the older group were subjects whose excretion level of vitamin C was considerably lower (37 patients, two to four times, and 33 patients less than twice, the preinjection value), thus indicating subnormal saturation levels, the patients of this group were more of the senescent type, some of them being well over 70 and some 80 years of age, a period at which the possibility of renal impairment of excretion, with or without the symptoms of renal insufficiency, must be considered.

The literature often contains data on vitamin C deficiency in connection with the formation of cataract, postoperative bleeding or retinal hemorrhages and authors even recommend therapeutic measures based on these findings. The deficiency was often established on plasma or blood levels or on the urinary excretion, in my experience, however, only the saturation test furnishes a quantitative index of the level of vitamin C nutrition. It must be regarded as erroneous to draw conclusions merely from a single determination of the vitamin C content of the urine. The saturation test disclosed, first, that there is no deviation in hemorrhagic diathesis, such as Werlhof's disease (thrombopenic purpura), Henoch-Schönlein purpura and hemophilia, only in some cases of so-called essential thrombopenic purpura is C-avitaminosis the etiologic factor.

The so-called intradermal test (Rotter, Portney and Wilkinson, Reddy and Sastry<sup>30</sup>), based on the intradermal injection of 2,6-dichlorophenolindophenol and the decoloration of the wheal produced under action of the ingested vitamin C, seems a less accurate method of determination than the saturation test.

Seefried<sup>31</sup> employed the saturation test with a small number of cataractous patients, administering 300 mg of ascorbic acid orally daily until the urine contained 150 mg of the vitamin. The cataractous patients needed a longer period of administration than the normal con-

<sup>29</sup> Ludden, J. B., and Wright, I. Effect of Renal Retention of Vitamin C on Saturation Tests. Formula for Compensation of This Factor of Error, *Arch Int Med* **65** 151 (Jan.) 1940.

<sup>30</sup> Reddy, D. V. S., and Sastry, P. B. Intradermal Test for Vitamin C Nutrition of Body in Ophthalmic Patients, *J Indian M. A.* **10** 440, 1941.

<sup>31</sup> Seefried, J. Ueber den Vitamin C-Haushalt der Alterstarkranken, *Arch f Ophth* **138** 620, 1938.

trols of the same age. He concluded that patients with senile cataract require for saturation a greater intake of vitamin C than control patients, the disturbance of the vitamin C metabolism of the entire body exerting a favorable influence for development of the opacities in the lens. Karbacher,<sup>32</sup> of Vogt's clinic found no significant difference in saturability with vitamin C between patients with cataracts and normal controls of the same age and he therefore expressed doubt of the presence of a systemic disturbance of vitamin C metabolism in patients with senile cataract. Urbanek employed the saturation test and measured the urinary excretion and the blood level of vitamin C, he found a higher excretion in the urine in the young than in the aged in spite of the activity of the former. The saturation level of the aged proved to be the same whether or not cataract was present, more vitamin C being necessary to reach saturation irrespective of the presence of cataract, the apparent diet is a more important factor vegetarians showing a lower degree of saturation. Gapeev arrived at a similar conclusion namely that the large amount of vitamin C in the aqueous and in the lens as compared with the low level in the blood of patients with cataract does not indicate any relationship. The aqueous of normal eyes showed 7.7 to 15 mg of vitamin C per hundred cubic centimeters, the lens 7.8 to 15.8 mg per hundred grams, the aqueous of cataractous eyes from 2.9 to 7.4 mg, the lens extracted by the intracapsular method 2.8 to 7.2 mg and the lens extracted by the extracapsular method 1.35 to 5.2 mg per hundred grams. The blood values for normal subjects were 0.3 to 1.2 mg and those for patients with cataract 0.8 to 0.46 mg per hundred cubic centimeters.

The human body is unable to synthesize vitamin C as some animals can and therefore depends entirely on an extraneous supply. Patients with some form of chronic illness, such as peptic ulcer, gallbladder disease and obstructive gastrointestinal lesions and often aged people with poor dentition and mastication confine their diet to soft well cooked foods, which are almost totally lacking in vitamin C. Their diets are especially deficient in orange juice, fresh fruits and raw vegetables the chief source of vitamin C. The average mixed diet maintains a normal vitamin C level, with little tissue reserve and a low urinary output. Depletion of vitamin C results either from an unbalanced

diet (lower intake) or from a disturbance of utilization, in the aged both possibilities must be considered, these persons may show a low blood level or a low urinary excretion of vitamin C which is not indicative of hypovitaminosis. The saturation test the measurement of the characteristic rise in excretion of vitamin C following intravenous administration of ascorbic acid, is the test indicative of a definite saturation level. In the case of patients responding with the typical increased excretion after intravenous administration of ascorbic acid, it may be assumed that the body is definitely at the saturation level. Only the group in which administration is not followed by an increase in urinary output within the next five or six hours can be considered as having a level of saturation below the normal, and therefore as belonging to the group with vitamin C deficiency. Undersaturation is present in a considerable proportion of the population and is often misinterpreted as the basis of various pathologic conditions. In my unselected series of patients the majority did not present any clinical deficiency of vitamin C, this is hardly understandable if hypovitaminosis C of the body is to be considered the underlying cause of the formation of opacities in the lens. In the smaller group the saturation test showed a degree of vitamin C deficiency which is often present with purpura and various pathologic conditions without having any significance undoubtedly being merely part of the general dietary deficiency. The more frequent occurrence of this deficiency in the higher age group speaks, rather, for the deficiency characteristic of senescence and not for any causal relationship to cataract formation. In spite of all the work done with vitamin C depletion of the body there is no conclusive proof that vitamin C deficiency is the cause of any disease other than scurvy. A dietary intake inherently poor in this substance or the presence of a disease with higher requirements of the vitamins such as febrile conditions, hyperthyroidism, malignant growths and leukemia, is accompanied with vitamin C deficiency. The vitamin C deficiency of some of the cataractous patients is a sequel to poor intake, poorer utilization and possible lower elimination of vitamin C by the kidneys and is characteristic of geriatric shortcomings.

Vogt<sup>33</sup> expressed himself as against the hypothesis that hypovitaminosis C is the cause of cataract, the hypovitaminosis is part of senescence, which only parallels and is coordinated with the formation of cataract. On the

32 Karbacher P. Kritische Bemerkungen zu Johannes Seefrieds Arbeit Ueber den Vitamin C-Haushalt der "Altersstarkranken." Arch f Ophth 140 748 1939

33 Vogt A. Zur Stardiskussion in Heidelberg, Klin Monatsbl f Augenh 101 530, 1938



basis of observations on aged identical twins, Vogt<sup>34</sup> concluded that senile cataract develops irretrievably and inevitably from the genetic anlage. In the same way in which the germ plasma is responsible for the life span of the organism (inheritance of longevity), it is the determining factor in the aging of the single organ. Accordingly, the senile cataract is similar to the forms of cataract representing genotypical or idiokinetic pathologic processes in the lens, and the differences of cataract formation in identical twins are quantitative but not qualitative. Von Szily<sup>35</sup> stated the belief that the assumption of absolute morphologic and genetic identity is unjustified. If senile cataract represents senile involution and premature dying of the lens, the premature senility, like altered basal metabolism depends not only on genes but on secretion of the gonads, the thyroid, the pituitary and the adrenal glands which influence and determine the individual type of aging. Vogt's contention that the senile cataract represents only the expression of heredity, and that therefore chemical studies must be futile, brought further objections from Krause,<sup>36</sup> who mentioned the amenability of hereditary diseases to therapy, for example, the treatment of diabetes with insulin and the use of thyroxine for hypothyroidism of identical twins. This dis-

cussion, the by-product of research on vitamin C as the causative factor in cataract, leads into the realm of genetics. One of the most common misconceptions of genetic laws seems to be the conclusion that if a character is conditioned by heredity it cannot be modified by environment. Hence, even if the concept of the hereditary basis of senile cataract were to be accepted, it would not exclude the possibility of environmental influences, of which metabolism, directly or indirectly (as vitamin C influencing the adrenal cortex), is only one of the numerous factors.

#### SUMMARY

The saturation test, the measurement of vitamin C output after intravenous injection of ascorbic acid is the most accurate index of vitamin C deficiency.

Of 200 unselected patients with cataract, 135 (62.5 per cent) revealed a saturation level of the body for vitamin C.

The rest of the series, 65 patients, showed a low level of vitamin C excretion after intravenous administration of ascorbic acid. In 35 patients (18.5 per cent) the deficiency was mild, and in 33 patients (16.5 per cent) it was more pronounced, representing a general deficiency.

There is not sufficient evidence to indicate that vitamin C deficiency contributes to the formation of cataract. Transparency of the lens is not dependent on the vitamin C saturation of the body, since the large number of senile cataracts associated with a normal saturation level would contradict such an assumption.

The vitamin C deficiency of some of the cataractous patients seems to be the natural result of the vitamin C deficiency of old age.

31 Lincoln Park

34 Vogt, A. Weitere Augenstudien an einigen Zwillingen höheren Alters über die Vererbung der Altersmerkmale, *Klin Monatsbl f Augenh* **100** 497, 1938.

35 Von Szily, A. Newer Aspects of Affections of the Lens, in Ridley, F., and Sorsby, A. *Modern Trends in Ophthalmology*, New York, Paul B. Hoeber, Inc., 1940, p. 436.

36 Krause, A. C. Medical Treatment of Senile Cataract, *Arch Ophth* **23** 487 (March) 1940.



# SYMMETRIC DEFECTS IN THE LOWER LIDS ASSOCIATED WITH ABNORMALITIES OF THE ZYGOMATIC PROCESSES OF THE TEMPORAL BONES

IRVING H LEOPOLD, M D , J FRANCIS MAHONEY, M D , AND MABEL LEE PRICE, M S

PHILADELPHIA

In 1888 Berry<sup>1</sup> described symmetric notches in the outer portion of the lower lids in a mother whose daughter had a similar defect in one lower eyelid. Although Berry did not examine the mother's brother, the latter reputedly had a similar defect in one eye. The affected child's brother had no ocular defect but a harelip, and her older sister showed no clinical defects



Fig 1—A, defects of the outer third of each lower lid in a 3 year old Negro girl. B, a close-up of the right eye of the same patient

In 1900 Treacher Collins<sup>2</sup> recorded 2 cases of symmetric congenital notching in the outer part of each lower lid associated with clinical evidence of defective development of the malar

Read before the College of Physicians, Philadelphia, Section on Ophthalmology, March 15, 1945

From the Departments of Ophthalmology, Radiology and Social Service of the Hospital of the University of Pennsylvania

1 Berry, G A. Note on a Congenital Defect (? Coloboma) of the Lower Lid, Roy London Ophth Hosp Rep **12** 255, 1888

2 Collins, T. Symmetrical Congenital Notches in Outer Part of Each Lower Lid and Defective Development of the Malar Bones, Tr Ophth Soc U Kingdom **20** 90, 1900

bones. The family history was negative for the condition in 1 case and was not mentioned in the other

In 1927 Isakowitz<sup>3</sup> described a similar case of symmetric notching of the outer portion of each lower lid. He stated the opinion that these defects were probably colobomas. Although he did not examine the father and sister of the patient reported on, studies of photographs indicated that they possessed the same symmetric defects of the lower lids. Isakowitz,<sup>3</sup> apparently unaware of the previous observations of Collins,<sup>2</sup> noted a depression of the orbital rim and suggested that a defect might exist in the zygoma. He did not examine his patient roentgenographically

In 1932 Waardenburg<sup>4</sup> mentioned a single similar case that he had observed but did not discuss any associated findings or the family history

In 1943 2 similar cases were reported by Mann and Kilner<sup>5</sup> and another by Johnstone<sup>6</sup>. Mann could find no ocular defects other than the involvement of the eyelid in the case which she reported, but she did present roentgenographic evidence of defective development of all the facial bones. The malar bones were very small and structurally malformed. Embryologically, Mann considers this type of case as one of retardation of differentiation of the maxillary mesoderm at and after the 50 mm stage. Kilner's<sup>5</sup> case was similar to that reported by Mann. However, his case history was more complete. As reported by Kilner, the affected child had a sister without any abnormality, and no family history of congenital defects was

3 Isakowitz, J. Eine seltene erbliche Anomalie der Lidspalte (atypisches Lidkolobom?), Klin Monatsbl f Augenh **78** 509, 1927

4 Waardenburg, P J. Das menschliche Auge und seine Erbanlagen, Haag, Martinus Nijhoff, 1932, pp 50-51

5 Mann, I, and Kilner, T P. Deficiency of Malar Bones with Defect of Lower Lids, Brit J Ophth **27** 13, 1943

6 Johnstone, I L. Deficiency of Malar Bones with Defect of Lower Lids, Brit J Ophth **27** 21, 1943

elicited Kilner's patient also had a harelip. No roentgenographic study was mentioned.

Johnstone's<sup>6</sup> case was similar, and roentgenographic changes showing poor development of the zygomas were noted.

Of these several papers, only Berry's<sup>1</sup> and Isakowitz's<sup>3</sup> suggest the hereditary nature of this lesion. The case reports of Mann<sup>5</sup> and Johnstone<sup>6</sup> include no family history. One of Collins's<sup>2</sup> cases, as well as Kilner's<sup>5</sup> case, as



Fig 2—Roentgenogram of a skull of 3 year old Negro girl, showing defects of the zygomatic processes of the temporal bones. Compare with the normal processes shown in figure 5.

recorded, appeared to be isolated instances in families with negative histories. Berry's<sup>1</sup> cases are not exactly similar to those observed later. His were the only cases in which the defect was unilateral, and he was unable to exclude the possibility of ocular trauma in the case of the mother's brother. He did not mention any abnormality of the facial bones.

In not one of the aforementioned reports was roentgenographic evidence of deficiencies of the zygomas sought for in other members of families of patients showing this symmetric defect of the lower lid. Such a malformation, if present, would be informative evidence of the hereditary nature of this defect.

#### REPORT OF A CASE

A similar case was recently observed in the ophthalmologic department of the Hospital of the University of Pennsylvania. V S, a 3 year old Negro girl, suffering from lead poisoning, was referred to the ophthalmologic service by the pediatric department. External examination revealed the marked deformity of both lower lids. The deformities were symmetric and involved the outer portion of each lower lid (fig 1). The underlying cheek appeared depressed on each side. The upper lids were

drawn down slightly at the outer canthi. The inner portion of each lower lid showed no lashes or meibomian glands (this defect was noted in the cases of Isakowitz and Mann). No other ocular abnormalities could be noted on external, biomicroscopic or ophthalmoscopic examinations. No deformities of the ears, lips or palate were observed, but the upper jaw appeared to be narrowed. In addition to suffering from lead poisoning, the child presented a behavior problem and was extremely uncooperative. Her obstreperous nature did not lend itself to roentgenographic study, and only after three attempts could satisfactory exposures be obtained. These roentgenograms revealed a defect of the zygomatic processes of the temporal bones (fig 2).

The roentgenologic report on the patient was as follows. The zygomatic processes of the temporal bones were absent bilaterally. There was no disproportion between the bones of the vault and those of the face and the base of the skull. The fontanels were closed, but there was a persistent frontal suture. The bones of the face were well developed, and the maxillary sinuses were large. The maxillary teeth were well developed and showed no malocclusion with the mandibular teeth. The zygomatic bones were normal.

The clavicles and the long bones showed no abnormality at this time. In the fall of 1944 the long bones showed evidence of lead lines in the metaphyses.

The ocular findings in this case resembled strikingly those reported by Collins,<sup>2</sup> Isakowitz,<sup>3</sup> Waardenburg,<sup>4</sup> Mann<sup>5</sup> (first case) and Johnstone<sup>6</sup>.

The mother and the maternal grandfather of the child displayed similar symmetric defects of the lower

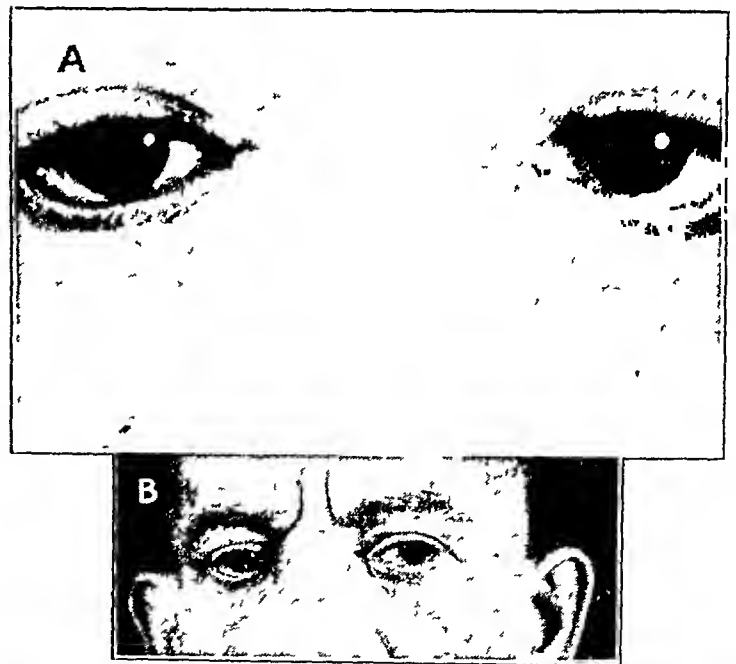


Fig 3—A, symmetric defects in the outer third of each lower lid in the mother of the child shown in figure 1. B, symmetric defects in the outer third of each lower lid of the grandfather of the same child. The defect has been altered by angular tarsorrhaphies, performed many years ago.

lids, with depression of the underlying portion of each cheek. The changes in the mother's lids were definite but not as pronounced as the child's. The grandfather's were evident but, again, were not as marked as the grandchild's. Angular tarsorrhaphies had been performed many years previously (fig 3 A and B). No disturbances of the lashes or of the meibomian glands were noted in the grandfather, but some reduction in the number of cilia and thinning of the lid existed in the

mother Both the mother and the grandfather had visual acuity in each eye of 6/6 without correction No other ocular defect could be found in either No deformities of the ears, lips or palate were present Roentgenographic studies revealed bilateral absence of the zygomatic processes in both the mother and the grandfather (fig 4)

The roentgenographic reports on the mother and the grandfather were as follows

arch may have been shorter than one normally sees

V S, aged 30, a Negro woman, had bilateral absence of the zygomatic processes of the temporal bones The bones of the vault appeared slightly larger than the bones of the base of the skull and of the face The maxilla was well developed, with good-sized maxillary sinuses, and the maxillary teeth were well formed, with no evidence of malocclusion with the mandibular teeth The zygomatic bones were well developed The clavicles showed no abnormality of development

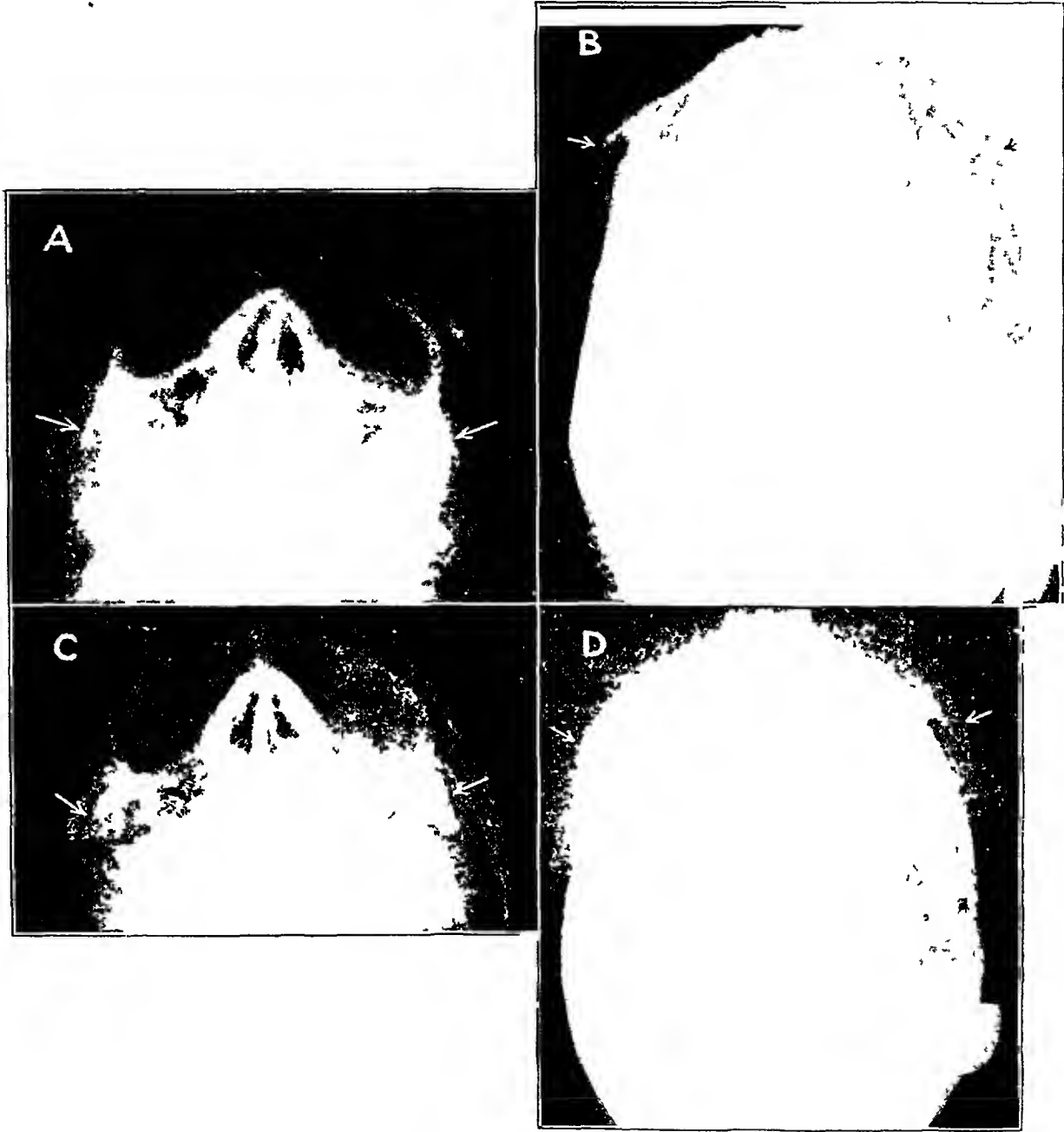


Fig 4—Two views of the head of the mother (A and B) and of the grandfather (C and D), showing bilateral absence of the zygomatic processes of the temporal bones In one view of the mother (B) the head is turned so that only one process can be clearly seen

S S, aged 50, a Negro, had bilateral absence of the zygomatic processes of the temporal bones The contours of the skull were not abnormal in that there appeared to be no disproportion between the bones of the vault and the bones of the face and the base of the skull The maxilla was normal, and the maxillary sinuses were well developed The tips of the zygomatic bones forming the anterior portion of the zygomatic

Careful inquiry, with the study of family photographs, revealed an interesting pedigree based on the abnormality of the lids (fig 6) The shaded figures in the chart represent members of the family with probable involvement, according to the information supplied by the mother and the grandfather, but for whom evidence was questionable because of lack of satisfactory photo-

graphs. The black symbols indicate members who were definitely affected as evidenced by the history and by photographs. All of the surviving members of the family are spread over the United States and either could not be reached or could not be induced to undergo an ophthalmologic or a roentgenologic study. It is possible that the child's uncle, who fails to demonstrate any significant defect of the lids, may possess deficient zygomatic processes.

The condition presented by this family is unquestionably a hereditary dysostosis but not a manifestation of the more common cleidocranial dysostosis. Fitzwilliams<sup>7</sup> said of the facial contour of the 40 patients with cleidocranial dysostosis whom he examined:

In every case where the skull changes are present they are accompanied by profound alteration in the skeleton of the face. The face itself [is] frequently described as small and small it is when compared with the normal. The disparity in size be-

comes was defects in the zygomatic processes of the temporal bones reported.

In the case reported by Mann,<sup>5</sup> considerable changes were shown in the facial bones, as well as in the sternum. The clavicles were not specifically mentioned. It is not possible from the evidence presented, to exclude her case from the cleidocranial dysostosis group. The case of Kilner<sup>6</sup> may also be of this type. Stocks<sup>8</sup> statistics reveal that in 55 per cent of the cases of cleidocranial dysostosis there were abnormalities of the palate. Kilner's<sup>6</sup> patient had a cleft palate. Unfortunately, roentgenographic examinations of the clavicles and of the facial bones were not included in the report.

In the reports by Berry,<sup>1</sup> Collins,<sup>2</sup> Isakowitz,<sup>3</sup> and Waardenburg,<sup>4</sup> the data were not sufficient to allow one to exclude their cases from the group with cleidocranial dysostosis.



Fig 5—Two views of normal zygomatic processes

tween the small face and large head is frequently well depicted in illustrations which accompany many of the published records of this condition. The supra-orbital ridges partaking in the increased girth of the cranium, prominently overhang the orbits, while the bones bounding the orbits below, in common with the majority of bones of the face, are small and ill-developed and appear flattened or sunken in comparison. The roof of the orbit is sometimes depressed, thus causing some degree of exophthalmos. The general aspect of the orbit resembles that of a patient with a mild degree of hydrocephaly.

Stocks,<sup>8</sup> in an analysis of 136 cases of cleidocranial dysostosis, stated that there were normal clavicles in only 2 instances. In none of these

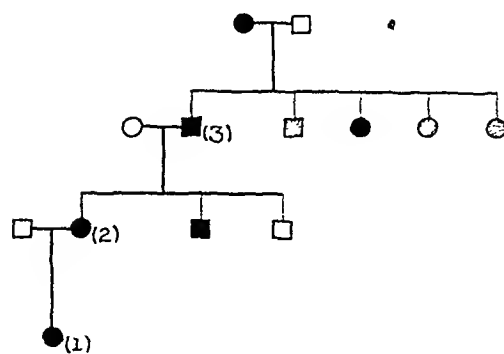


Fig 6—Pedigree of symmetric defects of the outer portions of the lower lids associated with bilateral absence of the zygomatic processes of the temporal bones. 1 indicates the child, 2, the mother, and 3, the grandparent, whose cases are described in the text.

The unshaded figures indicate that the lids were not involved, the black figures, that there was definite evidence of involvement of the lids, and the shaded figures, that the evidence was questionably positive (uncertain history and no photographs).

<sup>7</sup> Fitzwilliams, D. C. L. Hereditary Cranio-cleidodysostosis, *Lancet* 2: 1466-1475, 1910.

<sup>8</sup> Stocks, P., in Pearson, K. The Treasury of Human Inheritance. III. Hereditary Disorders of Bone Development, *Eugenics Laboratory Memoirs* 22, London, Cambridge University Press, 1925.

The pedigree in the present cases suggests that the responsible gene is a dominant one. Roentgenographic studies have established the fact that the deficiency of the zygomatic process is associated with the deformity of the lower lid and, in addition, have demonstrated that the osseous deficiency is similarly transmitted. The presence of normal facial bones, other than the zygomatic process of the temporal bone, and of normal clavicles would exclude these cases from the cleidocranial dysostosis group.

Although the defects of the lids in the 3 cases presented here are similar to those observed by Collins,<sup>2</sup> Isakowitz,<sup>3</sup> Mann and Kilner<sup>5</sup> and Johnstone,<sup>6</sup> the bony defects are chiefly of the zygomatic processes of the temporal bones, and not of the zygomas, as described in the other reports.

#### SUMMARY

Symmetric defects in the outer third of each lower lid, with absence of the zygomatic processes of the temporal bones, as shown roentgenographically, occurred in a grandparent, mother and daughter. The ancestral history of these cases suggests that the defect was hereditary and that the trait is a dominant one.

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#### DISCUSSION

DR FRANCIS MAHONEY, Philadelphia. There are numerous types and groups of dysostoses of the cranial bones. The commonest are the meningocele and the encephalocele, and less common is congenital absence of the superior orbital wall. In cases of the latter malformity there is a characteristic pulsation of the globe synchronous with cardiac pulsations. The least

common type of cranial dysostosis is *Luchenschadel*, or the lacework skull. This is the most severe and extensive of the dysostoses of the skull. None of these forms is hereditary.

Three types with a hereditary link have been reported. The defect represented by our cases is, I believe, the fourth type in this series. The most spectacular of these types, of course, is the hereditary cleidocranial dysostosis, in which cranial defects are associated with deficiency or absence of the clavicles. Some persons with this defect can bend forward and touch their shoulders together. They have, as Dr Leopold has described, changes in the facial bones, but these changes are in the maxilla, with deficiencies in the maxillary teeth and malocclusion with the mandibular teeth.

Another type is the hereditary craniofacial dysostosis. In this type changes in the skull and facial bones appear to be similar to those associated with cleidocranial dysostosis without the abnormalities of the clavicles.

The third type, which seems most closely related to the defect in our cases, is represented by the hereditary ectodermal dysplasias. In this condition there is a deficiency in the sweat glands and scanty or missing hair. Usually the upper incisor teeth are absent. The skull has the appearance of hydrocephaly, with a "too large head on a too small face."

In our cases the cranial bones are well formed. There is no disproportion between the bones of the vault and the bones of the face. There is no deficiency or malocclusion of the teeth. The clavicles are normal. The only osseous deficiency is the absence of the zygomatic processes of the temporal bones. However, the changes in the lower eyelashes and in the glands around them point to some link with the hereditary ectodermal dysplasias.

# VALUE OF CULTURES BEFORE OPERATION FOR CATARACT

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NEW YORK

A study of a series of 2,508 operations for cataract extraction was made to determine the value of preoperative cultures in the prognosis of postoperative infections and the influence of chemotherapy.

For the past eight years cultures of the eyes of patients admitted for cataract extraction have been examined for their bacterial flora. The purpose of this study was to determine whether any particular micro-organisms were responsible for postoperative infections. More recently these bacteriologic studies have been extended to aid in the evaluation of preoperative prophylactic chemotherapy.

## PROCEDURES FOR PREOPERATIVE CULTURES

In the cases reported the following uniform method was carried out. The patient was admitted a day prior to the cataract operation, and cultures of material from both eyes were made as follows: <sup>1</sup> Sterile cotton swabs, moistened in 1 per cent dextrose infusion broth were rubbed firmly twice (back and forth) over the greater part of the lower conjunctiva, carefully avoiding the lid border and the lashes. The swab was then immediately streaked over the surface of a rabbit blood agar plate. (The plate was divided into four portions—two for the cultures from the conjunctiva of each eye and the other two for the cultures from the lids.) For culture of material from the lids a swab was applied to the outer margin of the lid as the eye was held almost closed. Readings of the plates were made after eighteen and twenty-four and again after forty-eight hours incubation at 37 C. The cultures from the conjunctivas and the lids were worked out separately. The colonies present were counted and the types of colonies studied.

If a staphylococcus was found, the following steps were carried out to determine its pathogenicity:

1 *Fermentation of Mannitol*—Colonies of staphylococci from the original blood agar plate were transferred to a 1 per cent Difco-phenolsulfonphthalein-mannitol agar plate. Fermentation may occur within a two to three hour period of incubation at 37 C. The presence of acid is indicated by the change of color from red to yellow.

Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, Jan 15, 1945.

From the Department of Ophthalmology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology of Presbyterian Hospital.

1 Khorazo, D., and Thompson, R. The Bacterial Flora of the Normal Conjunctiva, *Am J Ophth* 18: 1114-1116, 1935. Thompson, R., and Khorazo, D. Susceptibility to Lysozyme of Staphylococci, *Proc Soc Exper. Biol & Med* 33: 299-302, 1935.

2 *Coagulase Test*—For this test fresh human plasma was used. The following procedure was carried out: Three-tenths cubic centimeter of plasma was mixed with a colony of staphylococci. The tube was incubated for four hours in a water bath at 37 C. Complete or partial coagulation after two to four hours indicates the production of coagulase.

Other types of organisms were isolated and identified by the usual bacteriologic tests.

## MATERIAL AND RESULTS

This study included only eyes on which a cataract operation had been performed. Because only rarely was but one organism present and because we had many varieties from the conjunctiva and the lid, it was necessary to make an arbitrary decision with regard to the patient's bacteriologic classification. The cases were grouped roughly as follows:

Group 1 consisted of cases in which hemolytic and nonhemolytic *Staphylococcus albus* was the predominating organism. These strains did not ferment mannitol or produce coagulase.

Group 2 consisted of cases in which so-called pathogenic *Staphylococcus aureus* was found, though it did not necessarily predominate. The pathogenic *Staph aureus* was defined by the fermentation of mannitol and the production of coagulase.

Group 3 consisted of cases in which so-called pathogenic *Staph aureus* was found, though it did not necessarily predominate. The pathogenic *Staph aureus* was defined by the fermentation of mannitol and the production of coagulase.

Groups 4, 5, 6, 7, 8, 9 and 10 consisted of cases in which the following organisms predominated: group 4, diphtheroids; group 5, *Pneumococcus*; group 6, *Streptococcus pyogenes*; group 7, *Streptococcus viridans*; group 8, *Proteus vulgaris*; group 9, *Hemophilus influenzae*; and group 10, miscellaneous gram-negative bacilli. Group 11 consisted of cases in which no growth occurred.

All variations of the bacteriologic pattern were found. In some cases one organism was present, in some three or more bacteria were present, and in others no growth occurred.

Our bacteriologic results and the correlation with the occurrence of purulent postoperative



infection are shown in table 1. The table presents the data for eleven groups of cases according to the organisms isolated. Group 1 was the largest and the predominating organism isolated was hemolytic or nonhemolytic *Staph albus*. The colonies presented morphologic variations. Some of the colonies were round and smooth, others had irregular edges and were opaque. A zone of hemolysis of from 1 to 2 mm occurred in

TABLE 1—*Correlation Between Preoperative Bacterial Flora and Postoperative Infection in 2,508 Cases in Which Neither Sulfonamide Drugs Nor Penicillin Was Used Preoperatively*

Group	Number of Operations	Organisms Isolated	Number of Postoperative Infections
1	1 705	<i>Staph albus</i>	None
2	529	Pathogenic <i>Staph aureus</i>	11
3	62	Unusual staphylococcus	None
4	86	Diphtheroids	None
5	20	<i>Pneumococcus</i>	None
6	9	<i>Strep pyogenes</i>	None
7	6	<i>Strep viridans</i>	None
8	16	<i>Proteus vulgaris</i>	None
9	2	<i>H influenzae</i>	None
10	18	Gram negative bacilli	None
11	52	No growth	None

some instances. The pigment production varied from the typical white color to a slightly greenish shade. The organisms were most numerous in cultures from the lids, although in some cases the growths from the conjunctiva and from the lids were equal. This group of staphylococci was considered nonpathogenic, since the strains did not ferment mannitol or coagulate human plasma. In these cases no serious postoperative infections occurred.

Group 2 was comprised of cases in which preoperative cultures showed pathogenic hemolytic or nonhemolytic *Staph aureus*. The colonial morphology was typical except for a few strains producing rough colonies. The hemolyzed zone was from 1.5 to 3 mm in width. The usual pigment was orange, otherwise it varied from slightly yellow to deep yellow. Some species did not produce hemolysis. The staphylococci in this group were considered pathogenic since the strains isolated fermented mannitol and produced coagulase. In this group postoperative infections with the *Staph aureus* occurred in 11 cases. In 6 of these cases the eye was removed, while in the remaining 5 cases the globe was retained but all vision was lost. There were other complications in this group, such as persistent conjunctivitis, corneal ulcer and iridocyclitis, which may possibly have been produced by this organism but they are not included in this report because of the difficulty in establishing the etiologic relationship.

Group 3 consisted of cases in which an atypical staphylococcus was the predominating organism. Strains isolated from the conjunctiva and the lids either fermented mannitol and did not produce coagulase or produced coagulase and did not ferment mannitol. The colonies isolated did not appear unusual when compared with those in the two groups previously described. No postoperative infection occurred.

Group 4 consisted of cases in which diphtheroids predominated. Some were identified as *Corynebacterium xerosis* and others as *Corynebacterium hofmanni*. We did not attempt to classify all the diphtheroids. These organisms appeared to be entirely nonpathogenic for the eyes and did not produce any postoperative infections. Groups 5, 6 and 7, consisting of very few cases, were those in which *Pneumococcus*, *Strep pyogenes* and *Strep viridans*, respectively, predominated. No infections occurred postoperatively.

In groups 8 and 9 typical *P. vulgaris* and *H. influenzae* were the predominating respective organisms, and postoperative infections did not occur.

In group 10 gram-negative bacilli were present which were not classified. The colonies were translucent, round and glistening and developed fully only after forty-eight hours' incubation. They were gram-negative slender bacilli, nonmotile, non-acid-fast and in some respects resembled diphtheroids morphologically. The strains isolated did not ferment any sugars and did not liquefy gelatin or Löffler's serum. Indole was not produced. Some strains produced acid, slight coagulation or digestion in litmus milk. Group 11 consisted of cases in which no growth occurred. In this group no postoperative complications occurred.

As seen in table 1, operation for cataract was performed in 529 cases in which pathogenic staphylococci were present. Since purulent postoperative infections occurred in only 11 cases, we thought that some specific surgical method might influence the incidence of postoperative infection. Several methods of cataract extraction were employed. The type most frequently employed was the intracapsular and next was the extracapsular extraction. Infection occurred in 5 cases after each of these types of extraction and in 1 case after a linear extraction. Therefore it seems that postoperative infection is independent of the type of operation.

Since these postoperative infections were due to pathogenic staphylococci, it seemed reasonable to investigate the possibility of developing a uniform preoperative procedure which could form the basis for treatment in the future. From

September 1943 to January 1944 two types of treatment to prevent postoperative infections were used. First, we applied an ointment (50 per cent hydrous wool fat and 50 per cent white petrolatum) containing sodium sulfathiazole in 5 per cent concentration three or four times daily to the conjunctiva and the lids until the pathogenic organisms disappeared. Repeated cultures determined the rate of progress of the treatment. It usually required from seven to ten days to eliminate the staphylococci, the period depending on the number of pathogens present on the lids and the conjunctiva. This treatment was discarded because of the frequency with which the patients exhibited an allergic response to this form of medication.

We then began using an ointment containing approximately 1,000 to 2,000 Oxford units of penicillin per gram of base (hydrous wool fat). After the isolation of a potential pathogen from the preoperative culture, this ointment was applied every two or three hours to the conjunctiva and the margins of the lids. The frequency of local application was based on the number of the bacteria present on the conjunctiva and the lids. Since penicillin deteriorates rapidly and also escapes from the eye, frequent treatments were considered necessary. In our opinion, it is not so satisfactory to use penicillin in drop form because in aqueous solution it disappears more rapidly from the conjunctiva and, furthermore, does not remain in constant contact with the eyelashes, where the greater number of organisms are usually found. To observe the rate of the clearing up of the infection, two cultures a day were taken—one in the morning and the other late in the afternoon. It was found that it required from three to eight days of constant treatment to eliminate the pathogenic staphylococci from the conjunctiva and the lids. This slow progress was confirmed by repeated cultures. In general the idea is to maintain the penicillin ointment constantly on the conjunctiva and the lids in order to inhibit the growth of the infecting organism. Each case presents an individual problem, depending on the number of organisms. In some cases a sensitivity to penicillin may develop, comparable to the sensitivity to the sulfonamide compounds. In such cases local treatment with penicillin ointment was discontinued. One patient appeared to be sensitive to the hydrous wool fat base.

All the strains of staphylococci isolated from the conjunctiva and the lids were tested for sensitivity to penicillin. The usual method of testing increasing dilutions of penicillin for its ability to prevent growth of a 1:100 dilution of

staphylococci proved the organisms to be sensitive to the drug.

In 663 cases of cataract encountered since January 1944, penicillin ointment has been applied routinely to both eyes as soon as the material for cultures was taken. Each patient, before his operation, received at least five treatments, even in the absence of the pathogenic staphylococci. In the presence of a pathogenic staphylococcus, the penicillin treatment was continued as previously described until the conjunctivas and lids were free, or almost free, of pathogens. In not all the cases in which operation was done after the treatments were the eyes entirely free of the pathogens. The final cultures still had a few colonies either from the conjunctiva or from the lid. In these cases penicillin dressing was applied immediately after the operation and in the subsequent dressings. This group also includes the clinic cases, in which often cultures were taken about a week prior to admission. Because of the scarcity of penicillin ointment, the clinic patients were given ointment containing 5 per cent of sodium sulfathiazole, to be used several times daily. On admission to the hospital they were given the routine treatment with penicillin ointment. In none of the 663 cases did a purulent infection occur.

For comparison, we collected data on 730 earlier cases in which no preoperative cultures were made. The preoperative treatment here consisted of "puddling" the eye with a fresh solution of protein silver (25 per cent) an hour or two before operation and again on the operating table. In some instances this same treatment was used the night before operation and early the next morning, in addition to the two treatments just prior to operation. The incidence of purulent postoperative infection in the two groups is shown in table 2.

TABLE 2—Incidence of Postoperative Infections in 730 Cases in Which Preoperative Cultures Were Not Made and Only Protein Silver Was Used Before Operation as Compared with Incidence in a Series of 663 Cases in Which Preoperative Cultures Were Made and Penicillin Ointment Was Used

Group	Number of Operations	Number of Infections	Preoperative Treatment
1	730	13	Protein silver, 25%
2	663	None	Penicillin ointment (1,000-2,000 Oxford units)

In 104 cases in which operation was delayed because of the presence of pathogenic organisms (as summarized in table 3) no infections occurred when this type of treatment was used.

preoperatively to rid the conjunctiva and the lids of the bacteria. Some patients appeared to be sensitive to sulfathiazole, so they were treated with penicillin. Two patients from the penicillin group were placed under treatment with sulfadiazine because the pathogenic staphylococcus isolated from the conjunctiva was not sensitive to penicillin. Four patients, 2 with *Str. pyogenes* and 2 with a pneumococcus, were successfully treated preoperatively with an ointment containing 5 per cent sodium sulfathiazole. As seen in table 1, 32 patients with either *Str. pyogenes* or a pneumococcus present in the eye were not treated and no postoperative infection occurred.

COMMENT

From this bacteriologic analysis it would appear that the presence of a pathogenic staphylococcus in the eyes previous to cataract extraction increases the possibility of postoperative infection. Of 529 eyes operated on with known pathogenic staphylococci present in the preoperative cultures, purulent postoperative infections occurred in 11. It seems, also, that the type of operation does not influence the occurrence of postoperative infection. It is interesting to note that the great majority of the patients with cataract whose eyes showed numerous pathogens had no postoperative infection. It is possible that variation of lysozyme content has a great deal to do with the natural defense of the eyes and their resistance to postoperative infections. \*Fleming<sup>2</sup> and Ridley<sup>3</sup> stated that some pathogens are affected by lysozyme. It may be that a high concentration of certain enzymes affords protection against any type of infection. It is known that lysozyme may inhibit and destroy saprophytes. Tears have a high concentration of lysozyme. When postoperative infections developed, they were usually due to the pathogenic *Staph. aureus*. However, it is interesting to note that in the group of patients for whom preoperative cultures were not made the postoperative infections were not all due to *Staph. aureus*. In 2 the infection was caused by a pneumococcus, in 1 by *Str. pyogenes* and in 1 by *Bacillus pyocyaneus*.

Before preoperative treatment with penicillin or sulfathiazole was instituted, it was routine to 'puddle' both eyes with 25 per cent protein

silver. Thompson, Isaacs and Khorazo,<sup>4</sup> in a study of the action of this disinfectant under conditions as similar as possible to those in the eye, found that protein silver is slow in action as an antiseptic against pathogenic organisms and that it is moderately injurious to leukocytic activity and definitely so to the action of lysozyme.

Recently all patients with pathogenic organisms have been treated preoperatively with penicillin ointment or with 5 per cent sodium sulfathiazole ointment (table 3). Our experiments

TABLE 3—Incidence of Postoperative Infections in 104 Patients Treated with Sulfonamide Drugs or Penicillin

Number of Patients	Organisms Isolated	Drugs Used	Number of Postoperative Infections
72	Pathogenic <i>Staph. aureus</i>	Penicillin ointment (1,000-2,000 Oxford units per gram)	None
28	Pathogenic <i>Staph. aureus</i>	Sodium sulfathiazole ointment, 5%	None
2	Pneumococcus	Sodium sulfathiazole ointment, 5%	None
2	<i>Str. pyogenes</i>	Sodium sulfathiazole ointment 5%	None

have shown that it is possible to free the conjunctiva of the pathogens in from three to ten days, and in some instances forty-eight hours is sufficient. While some patients normally carry pathogenic staphylococci in the conjunctiva or lids without any symptoms of inflammation and no infection develops if there is no surgical intervention, the presence of such pathogens in the eye may give rise to postoperative infection. Even this small series of patients treated locally with penicillin ointment shows such encouraging results that it should be possible to establish treatment in the future for patients whose conjunctiva and lids harbor pathogenic staphylococci. If this freedom from postoperative infection continues as the series is enlarged, the value of preoperative treatment is clearly suggested. It is interesting to note that in 27 of these 104 cases, foci other than the eye were found from which pathogenic staphylococci were isolated. These foci were in the throat, the nose and the skin around the eye. Adequate treatment of such foci may be necessary in order to prevent reinfection of the eye.

SUMMARY AND CONCLUSION

Great variation in the preoperative bacterial flora was observed in studies on 2,508 eyes

4 Thompson, R. Isaacs, M. L., and Khorazo, D. A Laboratory Study of Some Antiseptics with Reference to Ocular Application, *Am J Ophth* 20: 1087-1099, 1937

2 Fleming, A. On a Remarkable Bacteriolytic Element Found in Tissues and Secretions, *Proc Roy Soc, London*, s B 93: 306-317, 1922.  
3 Ridley, F. Lysozyme. An Antibacterial Body Present in Great Concentration in Tears, and Its Relation to Infection of the Human Eye, *Proc Roy Soc Med* 21: 1495-1506, 1928.

previous to operation for cataract. The predominating organism appeared to be *Staph. albus*, and the next in order pathogenic *Staph. aureus*. Other organisms occurred less frequently.

Postoperative infections were due in the great majority of cases to pathogenic *Staph. aureus*.

Postoperative infections observed were independent of the type of operation.

Of 730 cases in which no preoperative cultures were made and the treatment before operation consisted of instillation of protein silver, 25 per cent, three or four times in the twenty-four hours preceding operation, postoperative infection occurred in 13.

In 663 cases in which penicillin ointment (1,000 to 2,000 Oxford units), or sodium sulfathiazole ointment, 5 per cent, was used preoperatively, no infections occurred.

In 104 cases in which, because of known pathogenic organisms, operation was delayed until treatment with penicillin or sulfathiazole was used, no infections occurred.

This study indicates that preoperative cultures should be made on admission in every case in which cataract extraction is to be done, with a view to prophylactic treatment.

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#### DISCUSSION

DR ARNOLD KNAPP, New York. This is a valuable paper and shows a great advance in demonstrating that with certain preliminary

treatment of the eyes preparatory to cataract extraction the convalescence will proceed without infection. Formerly one used to examine a smear, and if only a few staphylococci were present, the operation was proceeded with, provided everything else was normal. First, I should like to ask whether the number of staphylococci is a factor in pathogenicity. Second, I should like to ask Dr. Dunnington in how broad a sense he uses the term "infection." Does it include any undue redness of the eye or mild iritis? These also are signs of infection.

DR JOHN DUNNINGTON, New York. I am glad that Dr. Knapp has brought up the question of what constitutes an infection, although I hoped I had made it clear that we included as "infections" only those conditions that went on to endophthalmitis or panophthalmitis. Most of the infected eyes were removed. All of them suffered complete loss of vision. We did not include as "infections" conjunctivitis, iritis, iridocyclitis or corneal ulcer, as there was genuine doubt as to whether we could identify the infecting organisms in such processes. In all of the cases listed as instances of infection cultures, both preoperative and postoperative, showed the infecting organism. We excluded purposely those in which there could be any question as to the nature of the infecting organism.

DR D. LOCATCHER-KHORAZO, New York. In answer to the question as to how many organisms can incite an infection, we have seen infection develop when only 3 colonies of pathogenic staphylococci were found preoperatively.

# CAVERNOUS DEGENERATION, NECROSIS AND OTHER REGRESSIVE PROCESSES IN OPTIC NERVE WITH VASCULAR DISEASE OF EYE

PROFESSOR ARNOLD LOEWENSTEIN

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Schnabel discovered cavernous degeneration in the tissue of the optic nerve in glaucomatous eyes. He<sup>1</sup> and his pupil Elschnig<sup>2</sup> declared that the condition was peculiar to glaucoma. Other investigators, like Axenfeld and Stock<sup>3</sup> found cavernous changes in the nerve in cases of high myopia. Koyanagi and Takahashi<sup>4</sup> and other authors observed the condition in eyes excised for intraorbital tumor. Lagrange and Beauvieux<sup>5</sup> demonstrated pronounced vascular changes in glaucomatous eyes which showed cavernous degeneration of the nerve. In several cases of primary glaucoma they discovered sclerosis and obliteration of the lamellar and retrolamellar vascular twigs in the optic nerve. It is interesting that they correlated cavernous degeneration of the optic nerve with similar features described in brain tissue in association with vascular disease called by Pierre Marie *état lacunaire* and by C. and O. Vogt *état criblé*. It is likewise interesting that Duke-Elder<sup>6</sup> stated that an ischemic factor attendant on sclerosis of the nutrient arteries may cause softening of the optic nerve tissue in glaucomatous eyes.

Several explanations of cavernous degeneration in the nerve have been advanced. The first is that the condition is the result of increased intraocular pressure. Another view has it that an abnormal lytic process is at work, the lysins being liberated in the intraocular fluid of glaucomatous eyes (Elschnig). My findings lead me to think

that these two views are untenable, for cavernous change is not limited to the prelaminar and the immediately postlaminar part of the nerve. For the most part the changes to be described are situated at some distance from the lamina cribrosa as well. A third view is that cavernous degeneration is the result of ascending degeneration in the nerve, a sequel of destruction of fibers at the disk associated with glaucoma. But, again, this cavernous change should present a continuity of the degeneration, and its intensity should be greatest near the disk and of lesser degree deeper.

I should like to stress that cavernous degeneration in the nerve is but one of the pathologic changes I have found in my study. The others were necrotic and sclerotic alterations. Thus, I found once ganglioform degeneration (cytoid bodies) and twice calcified hyaline concretions (diusen) within the tissue of the optic nerve. Sometimes indeed, two processes were demonstrable in one section. Once an area of fatty infiltration was noted. Profound vascular changes were present in all the eyes examined. Most of the eyes had been removed for thrombosis of the central vein complicated by glaucoma.

Glaucoma and vascular disease are closely associated in one's mind. Wagenmann<sup>7</sup> in 1892 stated the opinion that glaucoma and thrombosis of the central vein have a common cause. Salzmann,<sup>8</sup> after examining 65 eyes removed for absolute glaucoma found that only 8 had a normal central retinal vein. He assumed that thrombosis of the central retinal vein frequently follows primary glaucoma. He confirmed the opinion of Schweigger, Hirschberg, Coats, Leber, Verhoeft and others. Salzmann assumed that a chain of cause (increase of intraocular pressure) and effect (thrombotic vascular processes) aggravates the primary condition.

All the eyes examined were removed at operation, so postmortem changes can be discounted.

7 Wagenmann, A. Arch f Ophth 38 213, 1892

8 Salzmann, M. Glaukom und Netzhautzirkulation. Abhandlungen aus der Augenheilkunde und ihren Grenzgebieten. Berlin, S. Karger, 1933

From the Tennent Institute of Ophthalmology, Glasgow University (Prof. W. J. B. Riddell)

1 Schnabel, J. Arch f Augenh 15 311, 1885, Ztschr f Augenh 24 273, 1892

2 Elschnig. Glaukom, in Wessely, K. Pathologische Anatomie des Auges, in Henke, F., and Lubarsch, O. Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1928, vol 1

3 Stock, W. Klin Monatsbl f Augenh 46 342, 1908

4 Koyanagi, Y. and Takahashi, T. Arch f Ophth 115 596, 1924-1925

5 Lagrange and Beauvieux. Arch d ophth 42 129, 1925

6 Duke-Elder, W. S. Text-Book of Ophthalmology. St. Louis, C. V. Mosby Company, 1940, vol 3, p 3354



Not does the result of trauma to the nerve inflicted by forceps or scissors (Siegrist,<sup>9</sup> Elschnig and Goldberg,<sup>10</sup> Spuhler<sup>11</sup>) confuse the picture, for the effect of such injury bears no resemblance to the histologic changes described

#### REPORT OF CASES

CASE 1—The patient had a history of simple glaucoma, with trephination on Dec 16, 1939, and cataract. Absolute glaucoma developed in September 1940. The eye was excised.



Fig 1—A, necrotic focus in front of and cavernous degeneration behind the lamina cribrosa. Here, *a* indicates a necrotic focus, *b*, a patch of necrotic nerve fibers, *c*, an engorged capillary, *d*, cavernous degeneration, and *e*, border tissue.

B, longitudinal section of a branch of the central artery. The arrow shows narrowing of the lumen at the sharp edge.

Examination revealed a broad synechia at the root of the iris on one side, cellular infiltration of the iris and

<sup>9</sup> Siegrist, A. *Arch f Augenh (supp)* 44 178, 1901.

<sup>10</sup> Elschnig, A., and Goldberg, H. *Klin Monatsbl f Augenh* 40 (pt 2) 81, 1902.

<sup>11</sup> Spuhler, O. *Arch f Ophth* 56 77, 1903.

ciliary body, occlusion of the pupil with pigmented organized tissue, engorgement of all uveal vessels, and extensive mossy hemorrhages in the periphery of the retina (the retina was examined in bulk). In antero-posterior sections the retinal cup was filled with glial tissue. There were small foci of cavernous degeneration in front of the cribriform plate and a necrotic process (fig 1 A). The necrotic area (*a*) was sharply delineated, measured 80 by 100 microns and lay on the lamina

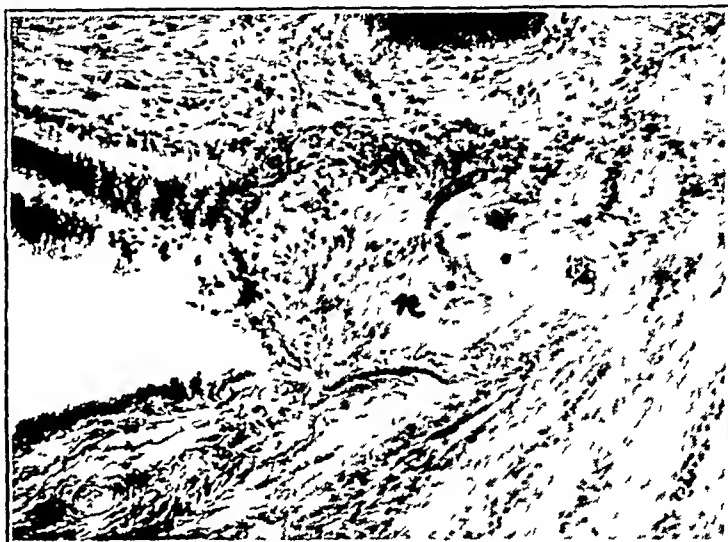


Fig 2—Necrotic prolapse of optic tissue between the retina and Bruch's membrane, *n* indicates a necrotic patch.



Fig 3—Four necrotic patches 1, 2, 3 and 4 in the lateral part of the optic nerve.

It reached the edge of the disk and was lined with what Elschnig has called "border tissue." A bundle of ill defined nerve fibers (*b*) was separated from the necrotic focus by infiltrated nerve fiber tissue. The walls of some of the small vessels in the nerve, as well as in the choroid, showed hyaline thickening. Behind the lamina there was extensive patchy cavernous degeneration (*d*). Figure 1 B, from the same eye shows narrowing of the lumen of a branch of the central



artery, from a diameter of 45 microns to one of 9 microns. The vessel is again dilated to a lumen diameter of 65 microns as it crosses the sharp edge of the cup.

**CASE 2**—In the affected eye, thrombosis of the central retinal artery had occurred. The iris was atrophic and the retina hemorrhagic throughout, with cystic degeneration. The choroidal vessels were much engorged. All the vessels showed broad hyaline thickening of the walls. The retinal cup was filled with glial

largely necrotic. A vessel could be seen coursing around the end of Bruch's membrane, and this vessel showed endothelial proliferation. Around the necrotic area were several rows of glial cells and engorged capillaries. Elsewhere in the nerve, behind the lamina (fig 3), were four necrotic patches. Partially or completely closed vessels were frequent in the neighborhood of these foci. The necrotic patches differed from the Siegrist-Elschnig artifacts.

**CASE 3**—This case, again, is an instance of thrombosis of the central retinal artery with secondary glaucoma. Iridectomy was performed, without success. The eye was excised. The whole uvea was infiltrated, and the choroid was thickened to five or six times normal. The walls of the vessels of the choroid were broad and hyalinized, and many vessels in the retina, as well as in the choroid, showed fatty necrosis of the subendothelial layer. Sections stained with sudan III showed fatty masses in the outer molecular layer and in the optic nerve. In pyroxylin sections the optic nerve was richly infiltrated with lymphocytes and showed a mi-

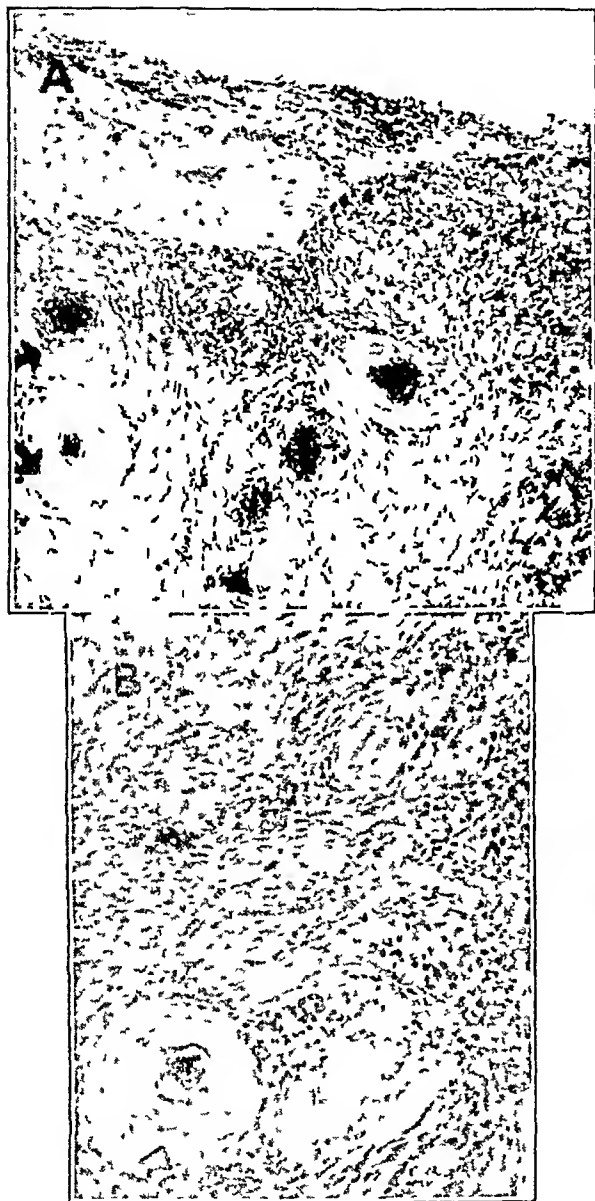


Fig 4—*A*, atheromatous vascular changes and cavernous degeneration. The arrows indicate atheroma vasculare.

*B*, high degree of thickening of the wall of the central retinal artery (arrow), surrounded by an area of cavernous degeneration. Note the ratio of lumen to wall of 1:2.

tissue and was bridged by a thin glial membrane. In figure 2, fibrous tissue with necrotic patches (*n*) can be seen to have invaded the area between Bruch's membrane and the retina, the layers of the latter having been raised in the process and destroyed at this side. This wedge of tissue was 225 microns in length and 170 microns in height. The center of this mass was



Fig 5—Cross section of the optic nerve behind the lamina cribrosa, showing the thrombosis of the central vessels. Weigert's elastica stain. Here, *a* indicates thickened perivascular coat, *b* a thrombosed vein, arrow at right, a sclerosed plaque, and arrow at left, cavernous degeneration.

nute, but widespread, "cavernous" change, giving the tissue a sieve-like appearance (fig 4 *A* and *B*). This change was not typical of cavernous degeneration but suggests fatty droplets dissolved in processing.

**CASE 4**—The eye was seen in a stage of absolute glaucoma demanding excision. The patient suffered from associated cerebral vascular disease. Figure 5 shows extensive retrolaminar cavernous change. The process involves more than one third of the radius of the disk. There were two large cavernous areas of this type, which were not linked, as serial cross sections of the nerve proved. Figure 5 shows also a sclerosed plaque separated from the cavernous area by healthy tissue. The plaque is surrounded by thick elastic fibers. There was thickening of the pia and arachnoid, with subdural hemorrhages in the sheath of the optic nerve.

CASE 5—This case was one of advanced hypertensive retinopathy with widespread hemorrhages in all layers of the retina, fatty infiltration of the retina, ganglioform degeneration of the retinal nerve fiber layer and bilateral retinal detachment. The vessels showed marked endothelial proliferation and subendothelial fatty necrosis. The disk was swollen asymmetrically. The nerve fiber layer was thickened locally near the disk, a growth of glial cells being responsible (fig 6 A). At the base of the swollen disk was a calcified, hyaline concretion, a so-called druse, measuring about 140 by 240 microns, staining dark blue and pushing the nerve fibers aside (fig 6 B). Many of the nerve fibers ended blindly

The cytoïd bodies did not take stains for fat. In this case different types of tissue degeneration were found existing simultaneously: necrotic, cavernous, ganglioform and hyaline.

CASE 6—This case was one of absolute glaucoma with iridocyclitis. The cornea, iris and ciliary body were infiltrated with lymphocytes and plasma cells. The root of the iris was adherent to the corneoscleral tissue. Strands of the vitreous with polymorphonuclear leukocytes and lymphocytes were observed. There was a preretinal capillary plexus, and extensive hemorrhage occurred throughout all layers of the retina. The septums and the sheaths of the optic nerve were in-

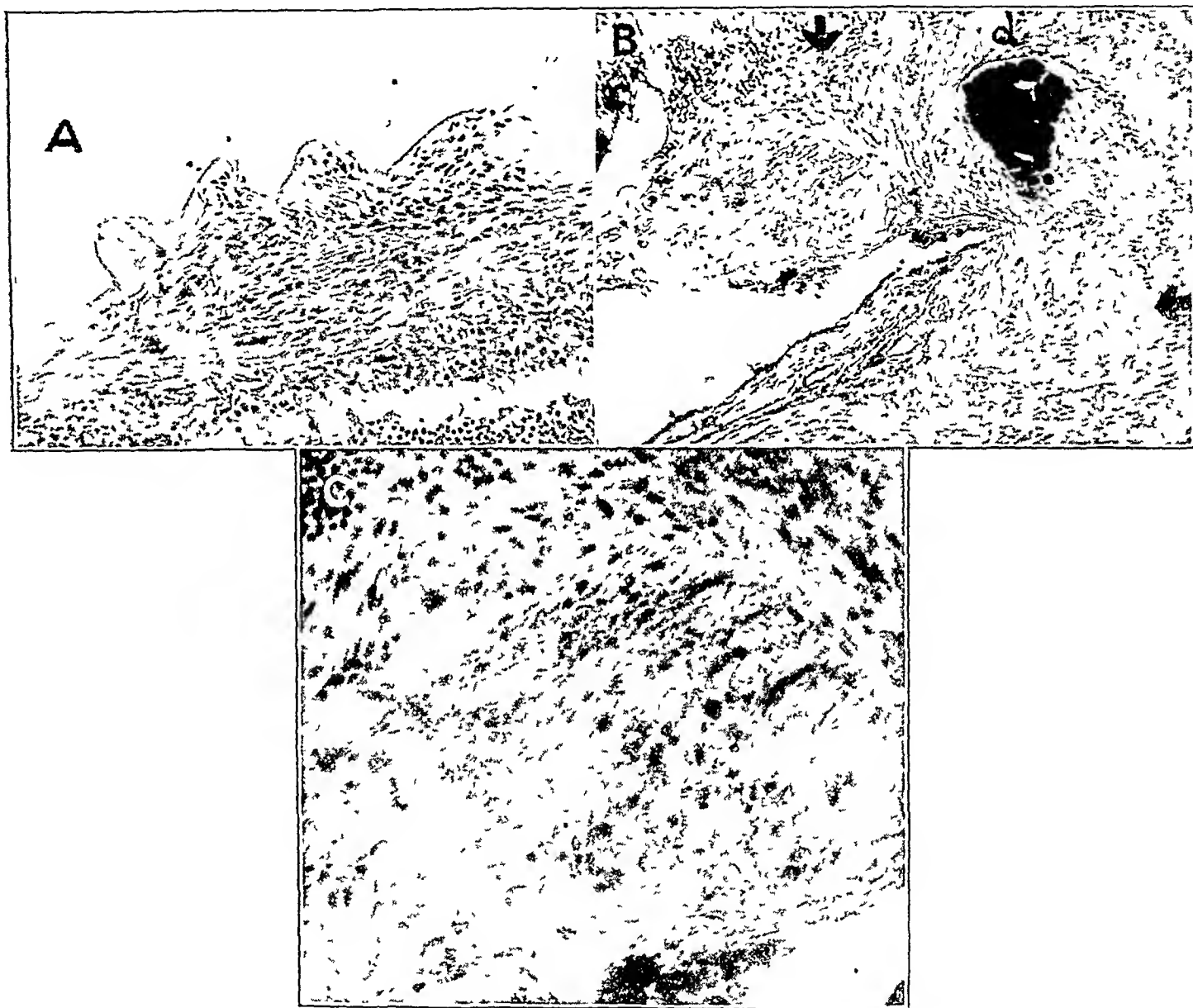


Fig 6—A, wavy protuberances near optic disk. The nerve fiber layer is thickened, and the glial nuclei are increased. B, subretinal prolapse of the nerve fibers which have undergone ganglioform degeneration (arrow at top) with calcified druse (*d*), or hyaline concretion, and cavernous degeneration (arrow at right). The retina is indicated by *r*. C, subretinal ganglioform degeneration of nerve fibers. Note the isolated nerve fibers diving into the necrotic mass. High power magnification.

here. Small foci of cavernous degeneration appeared between the druse and the lamina. An area between the raised retina and the choroid was filled with a wedgelike mass of degenerated nerve fiber tissue. The cross section of this wedge was a triangle, with a length of 920 microns and a height of 270 microns. The mass consisted of poorly staining granular material with cytoïd bodies. These bodies varied in size and the "pseudo nuclei" in staining reaction (fig 6 C).

filtrated with lymphocytes. Necrotic foci occurred in front of the lamina, some 7 to 800 microns long by 3 to 400 microns broad (fig 7 A and B), sharply demarcated and showing yellowish white in slides stained with hematoxylin and eosin. Around these foci was a framework of glial cells and fibroblasts. Most of the foci were structureless, granular masses. One focus sent a hornlike process between the retina and the pigmented epithelium, and at its outer limit it

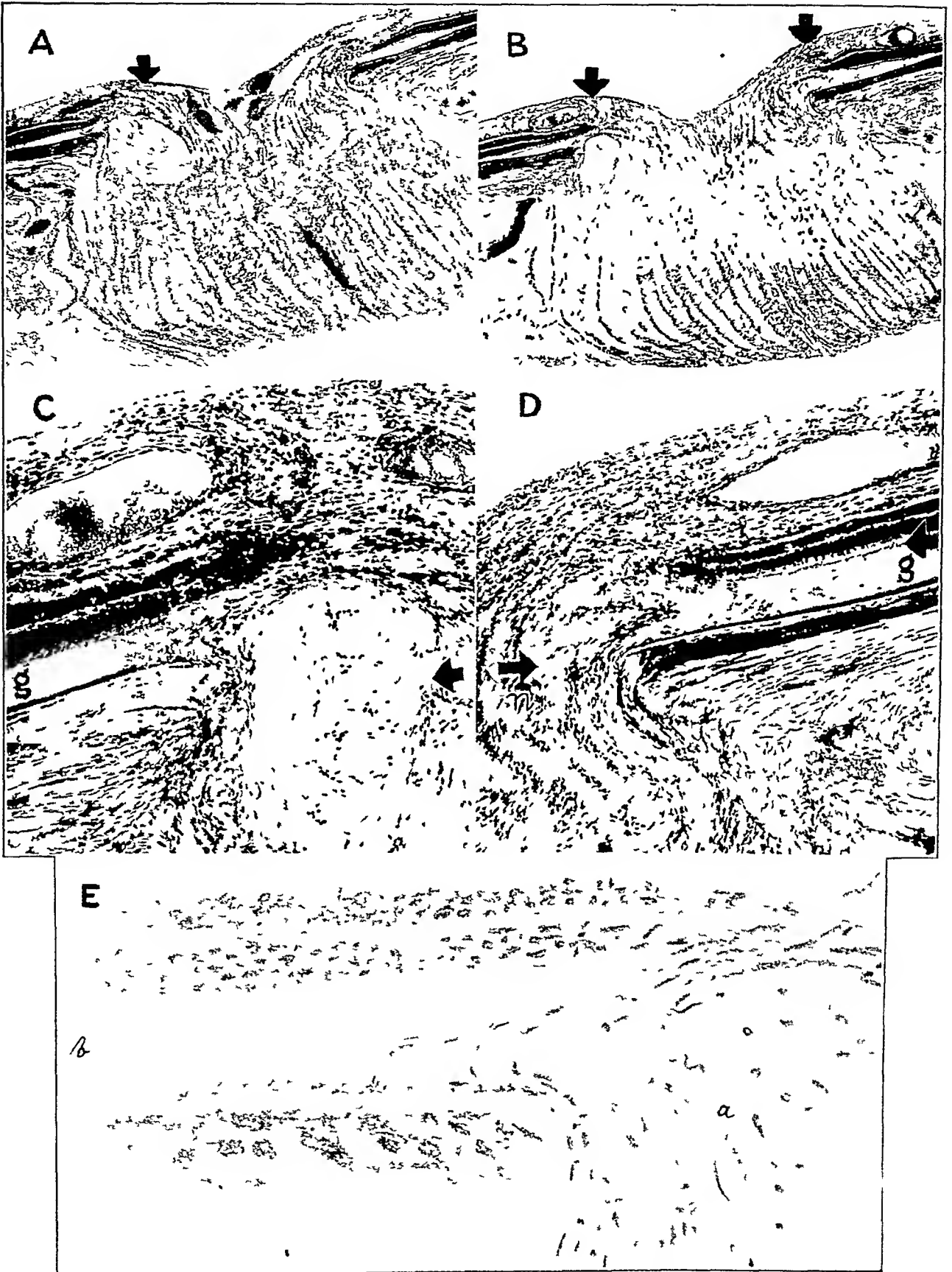


Fig 7—*A*, necrotic foci in the disk in front of the cribriform plate. The arrow indicates a sharply delineated necrotic focus with subretinal prolapse. *B*, necrotic foci (arrow at left) passing over into a subretinal necrotic mass (arrow at right). *C*, high power magnification of the necrotic focus (arrow at right) passing over into subretinal granular mass (arrow at left). *D*, nuclei of nerve fibers (*n*) turning sharply under the retina and ending abruptly within the necrotic layer. The arrow indicates normal neuroepithelium, *g*, the subretinal granular mass. *E*, necrotic mass (*a*) sending four processes into the subretinal granular mass (*b*),  $\times 600$ .

was bound by a structure having a laminated arrangement, like the layers of an onion (fig 7 C and E). The foci at the other side of the disk were not so sharply differentiated. There was an extension of granular necrotic substance subretinally. Here rows of elongated nuclei were freely embedded (fig 7 D). The existence of an extensive retinal rete mirabile and the large retinal hemorrhage are, I think, evidence that venous obstruction was present in this case.

Several other eyes excised for glaucoma were examined histologically, but the details of the findings need not be given. Some of them showed degenerative changes in the nerve, mostly cavernous and necrotic, associated with profound vascular changes.

#### COMMENT

Two points engaged my attention as the result of the study of these 6 cases. The first, and less significant perhaps, is the occurrence of subretinal prolapse of optic nerve tissue as a result of disease processes in the nerve. This may be consequent on the growth of aberrant nerve fibers, such as I have described elsewhere (Loewenstein<sup>12</sup>). In that study, the aberrant nerve fibers were found growing out from the nerve into the retroretinal area in an eye excised for a melanotic growth. It is interesting to speculate that the pathologic outgrowth of nerve fibers and the melanoma may have sprung from one stem, namely, an abnormal neuroectoderm, if Masson's concept is correct. Another concept more to the point is the origin of this prolapse of optic nerve tissue, such as occurred in case 5 (hypertensive neuroretinitis). It is suggested by a consideration of the changes that take place in papilledema. Paton and Holmes<sup>13</sup> have shown that the optic nerve fibers sometimes push aside and raise the retina in the neighborhood of the swollen disk. B. Samuels<sup>14a</sup> has distinguished three types of circumpapillary tissue in papilledema: (1) a more or less homogeneous mass, similar to a coagulated fluid, (2) a very loosely meshed tissue, poor in nuclei, and (3) a compact, very cellular tissue, reminding one of neuroglia proliferation. Abelsdorff,<sup>14b</sup> in similar observations, described the fibers at the edge of the swollen disk as assuming an S-shaped band. Paton and Holmes were able to demonstrate an actual rupture of the fibers in this lateral bulge. I did not note rupture of the fibers in 6 cases of papilledema, other than in case 5, in which I ex-

amined the eyes. In 1 case only a broad wedge of optic nerve fibers was found between the hexagonal cells and the retina. It would seem, however, that in case 5 (hypertensive retinopathy) rupture of the fibers really took place in passing over the sharp edge of the calcified mass. The rupture may have been due to the mechanical effect of the lesion.

The second, and major, point of interest is the variety of forms of degeneration appearing consistently in the nerve in association with profound vascular disease. Various degenerative processes were often present contemporaneously. Necrotic and cavernous patches were frequently associated. Case 4 is especially interesting, as several cavernous foci occurred, with a sclerosed plaque. Small vessels of the optic nerve showed changes in the walls and thrombotic occlusion. This association was stressed recently by Schemker,<sup>15</sup> who demonstrated that the sclerosed plaques in the brain in cases of acute disseminated sclerosis are frequently associated with thrombosed vessels.

I want to mention especially the findings in case 3, in which fatty infiltration of the optic nerve tissue was discovered with the sudan III stain. Pyroxylin sections of the other part of the optic nerve displayed rarefaction of the tissue, similar to cavernous changes.

Henschen<sup>16</sup> found malacic and necrotic changes associated with arteriosclerosis. He demonstrated them in the occipital lobe and elsewhere. Fuchs<sup>7</sup> discovered focal degeneration in the optic nerve in cases of arteriosclerosis. The foci appeared as granular masses in section without inflammatory reaction. Fuchs stated that they were consequent on disturbance of the small pial twigs supplying the nerve. In the histologic literature on toxic neuritides, e.g., those due to alcohol and diabetes, vascular changes are frequently mentioned (Igersheimer<sup>18</sup>). I think that the changes I have found in the optic nerve—cavernous, necrotic, ganglioform and sclerosed degeneration and establishment of calcified drusen—were secondary to vascular disease.

#### SUMMARY

A histologic study was made of several eyes with profound vascular changes. Special attention was given to the pathologic types of degen-

12 Loewenstein, A. *Brit J Ophth* **29** 6, 1945.

13 Paton, L., and Holmes, G. *Tr Ophth Soc U Kingdom* **31** 117, 1911, *Brain* **33** 389, 1911.

13a Samuels, B. *The Histopathology of Papilloedema*, *Tr Ophth Soc U Kingdom* **57** 529, 1938.

14 Abelsdorff. *Optic Nerve*, in Wessely, K. *Pathologische Anatomie des Auges*, in Henke, F., and Lubarsch, O. *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1928, vol 1, p 725.

15 Schemker, I. M. *Histogenesis of Early Lesions of Multiple Sclerosis. Significance of Vascular Changes*, *Arch Neurol & Psychiat* **49** 178 (Feb) 1943.

16 Henschen, S. E. *Arch f Ophth* **78** 212, 1911.

17 Fuchs, E. *Arch f Ophth* **103** 304, 1920.

18 Igersheimer, J. *Am J Ophth* **23** 1243, 1940.

eration in the optic nerves. The observations on 6 eyes are described in some detail.

Cavernous and necrotic degeneration were almost consistently found and frequently the two changes occurred together. They were sometimes present in marked degree, at others they were inconspicuous. A sclerotic plaque, a subretinal process of gangliform degeneration of nerve fibers and, in 2 cases, a calcified druse were found in the optic nerve.

In some cases the disease process exceeded the boundaries of the nerve head and extended into the subretinal space.

These observations lead me to conclude that all these degenerative changes are the result of vascular damage with impairment of nutrition rather than the effect of increased intraocular pressure.

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# EFFECT OF ANOXIA ON HETEROPHORIA AND ITS ANALOGY WITH CONVERGENT CONCOMITANT SQUINT

FRANCIS HEED ADLER, M D

PHILADELPHIA

In a previous paper<sup>1</sup> the existing knowledge of the voluntary and motor mechanisms controlling ocular movements was summarized. It was pointed out that the reflex mechanism was even more important than the voluntary, in that the eyes were constantly under the influence of involuntary tonic impulses which determined not only their fixation of objects in space but also their relation to each other. This mechanism is the harness which keeps the eyes associated so that the two maculas are used simultaneously.

The chief source of reflex tone is the visual fixation reflex. Lancaster<sup>2</sup> pointed out some time ago the importance of this mechanism for fusion, although he considered that it was a conscious, voluntary mechanism and traced the afferent pathway from the frontal centers instead of from the optomotor center in the occipital cortex. The evidence I believe is strongly in favor of its being a purely involuntary reflex.

All of the other sources of tone, such as the otolith apparatus, the semicircular canals, the convergence mechanism, and perhaps others as yet undiscovered, together with the visual fixation reflex suffice to keep the eyes in alignment with each other and fixed on an object in space which falls within the visual and motor fields. When the visual fixation reflex is artificially eliminated by one means or another and the position of the eyes is measured one is determining the effect of all these other sources of tone working together. This is spoken of as the measurement of the muscle balance, which, as Lancaster aptly remarks, puts the emphasis on the wrong part of the neuromuscular apparatus. I cannot do better than quote from Lancaster's admirable paper as follows:

He [the average ophthalmologist] sees an exophoria and says that the lateral rectus muscles are pulling too

From the Hospital of the University of Pennsylvania

Address delivered before the New England Ophthalmological Society, Boston, Feb 20, 1945

1 Adler, F. H. Pathologic Physiology of Convergent Strabismus. Motor Aspects of the Nonaccommodational Type, *Arch Ophth* **33** 362 (May) 1945

2 Lancaster, W. B. Physiology of Disturbances of Ocular Motility, *Arch Ophth* **17** 983 (June) 1937

hard or that the mesial rectus muscles are not pulling hard enough, which is true. But he jumps to the naive conclusion that the former muscles are too strong or the latter too weak, whereas the muscles are probably faithfully carrying out the orders brought to them by the nerves. The nerves, for their part, are merely transmitting the impulses from the nuclei, and the nuclei are issuing only such orders to contract or to relax as the messages from the supranuclear centers call for.

Any part of this neuromuscular mechanism may be out of order, and more than one part may be affected. But is it not reasonable to think that the most complicated part is the most likely to be acting imperfectly? When the patient is put through a course of orthoptic training, is it reasonable to suppose that the chief factor is a strengthening of the muscles already one hundred times as powerful as the task calls for? Does Paderewski play the piano so much better than another person because his muscles are stronger?

He also says

The sum of the matter is that nerve stimuli are constantly flowing to the extra-ocular muscles, and the stream varies with varying conditions. The resultant tonus or contraction of the twelve muscles does not produce a perfect balance, and the fusion faculty has to correct any shortcomings. When fusion is eliminated the ophthalmologist is able to see how much work the fusion faculty was doing before he covered one eye or otherwise eliminated fusion. This is the important thing about heterophoria—it shows what the task of the fusion faculty is. The measurement of the amplitude of fusion shows the capacity of the fusion faculty to deal with this.<sup>3</sup>

One must conclude therefore that heterophoria is an indication that the remaining reflex sources of ocular muscle tone have failed to keep the eyes in perfect alignment when the fusional mechanism is eliminated. Orthophoria, the ideal condition, is probably never found in all the positions in which the eyes are habitually used, and should therefore not be thought of as the normal condition. The limits within which there may be deviations from this ideal without symptoms are well recognized clinically, however, and it is certainly too much to expect ocular comfort in a person whose fusional impulses have to keep under control a latent deviation of the visual axes of more than 1 prism diopter in the vertical, or of more than 4 in the horizontal, plane for distance.

<sup>3</sup> Lancaster,<sup>2</sup> p 991



Since fusion is imperfect at birth the position the eyes assume until this mechanism develops into full maturity is usually a heterophoric position. It can easily be determined that at this period all the sources of reflex tone are active and variable and seldom are sufficient to hold the eyes in alinement. Frequently the eyes will deviate from one another during the first year of life, one eye remaining fixed while the other moves out or in or in the vertical direction. These movements are slow, steady deviations, which betrays their reflex nature.

If fusion should never develop the position assumed by the eyes would be that dictated by the remaining sources of reflex tone. It would not be the so-called position of rest, which occurs only during deep sleep, anesthesia or death. This position, which is generally divergence and some sursumvergence, never occurs as a result of elimination of the visual fixation reflex alone. This fact and a great many others which need not be mentioned here should throw doubt on the importance of a deficiency or absence of fusion as the primary cause of comitant strabismus. It is true that strabismus may not occur because of good fusion, in which case the condition will remain a heterophoria throughout life. But the absence of fusion without a preexisting heterophoria will never produce squint. The primary cause of squint is heterophoria, and by definition comitant strabismus is a manifest heterophoria.

The search for the cause or causes of squint therefore resolves itself into a search for the cause of the heterophoria. In the case of the lateral squints this must be sought in disorders of the convergence and divergence mechanism. Unfortunately, little is known of these mechanisms, even of their anatomic pathways.

There is no known frontal center for either convergence or divergence, although convergence certainly can be initiated volitionally. Involuntary convergence and divergence can easily be demonstrated under the influence of the visual fixation reflex, by merely inserting small prisms base in or out in front of one eye while looking at a muscle light. Without any effort on the subject's part the eye will immediately make an inward or outward movement in the interest of fusion until the image lies on the macula once more. This movement is involuntary—it cannot be prevented even by a willed effort. The largest prism which still effects this movement reflexly is the measure of the reflex fusional convergence or divergence.

Practically nothing is known of the normal physiology of the convergence and divergence mechanism and even pathologic conditions have

served to throw little light on its function. Convergence spasm usually occurs in neuros-thenic persons,<sup>4</sup> but the mechanism which seems to be at fault here is the voluntary convergence rather than the reflex mechanism. Divergence paralysis is a recognized clinical entity, but since most of these patients eventually show paralysis of both external rectus muscles one cannot be sure that a separate divergence mechanism is concerned.

The association of convergence and accommodation during the act of looking at close objects develops a normal linkage between these two functions. An abnormal amount of hyperopia calls for excessive convergence and readily explains the development of the esophoria which leads to accommodative convergent squint. About one third of convergent squints are purely accommodative. Another third have an accommodative element, but are probably not due solely to an abnormal hyperopia. There remain nearly a

Flight Schedule

	Feet	Meters
7 34 p m	started ground level	
7 35 p m	2,000	600
7 36 p m	7,000	2,100
7 37 p m	12,000	3,600
7 45 p m	16,000	4,800
8 26 p m	18,000	5,400
8 52 p m	descent started	
9 44 p m	3,000	900
9 47 p m	0 ended	

third of the cases of convergent squint which are not paralytic and which, like the accommodative squints, are due to an abnormal tonic convergence. The reason for this abnormal tonus is unknown, however.

It has been known for some time that under the influence of alcohol there develops an increasing esophoria, which eventually may be sufficient to overcome the fusional fixation reflex and produce esotropia. This occurs in all persons, regardless of whether they were orthophoric, esophoric or exophoric before partaking of the alcohol. Carefully controlled studies have been reported by Powell<sup>5</sup> and by Colson.<sup>6</sup> These authors are not decided as to the cause of the esophoria, whether it is due to an increase in

4 Souders, B. F. Hysterical Convergence Spasm, *Arch. Ophth.* **27** 361 (Feb.) 1942.  
5 Powell, W. H., Jr. Ocular Manifestations of Alcohol and Consideration of Individual Variations in Seven Cases Studied, *J. Aviation Med.* **9** 97 (June) 1938.  
6 Colson, Z. W. Effect of Alcohol on Vision. Experimental Investigation, *J. A. M. A.* **115** 1525 (Nov. 2) 1940.

convergence tone or whether there is a weakness of the divergence mechanism

A similar development of esophoria has been found to occur from the effect of anoxia by Velhagen.<sup>7</sup> Working in a low pressure chamber he found that the muscle balance changed in the direction of esophoria as the atmospheric pressure was reduced, no matter what the subject's phoria was to begin with. Since this was contrary to what Berens and Wilmer<sup>8</sup> had previously reported, I decided to repeat these experiments. The latter authors had found that anoxia merely increased any phoria which was

reflex was then measured for both convergence and divergence, care being taken to measure the reflex vergences only and not the voluntary ductions. (The reflex vergences are measured by inserting prisms of increasing strength in front of one or both eyes while both are fixing a distant light. When the subject first sees two lights without making any effort to fuse them the strength of prism used is the measure of the reflex vergence.) The fusional amplitude of each subject was then measured on the orthoptoscope. (The fusional measurements were all made by Miss Elizabeth Jackson, the Orthoptic

TABLE 1—Data for All Tests Except Those of Fusional Amplitude

Name	Altitude, Feet	Distance Maddox Rod		Near Maddox Rod		Near Maddox Wing		Ductions	
		Eso phoria	Exo phoria	Eso phoria	Exo phoria	Eso phoria	Exo phoria	Abduc- tion	Adduc- tion
Crandall	0	3.5		3.5		0	0	9	30
8 12 p. m.	16,000	5.5		0	0		1	8	40
8 48 p. m.	18,000	8		1		0	0	5	40
9 51 p. m.	0	4		2.5		0	0	10	36
Mayock	0		1		1		3	6	18
7 57 p. m.	16,000	1		0	0		2	5	16
8 39 p. m.	18,000	3			1		1	6	18
9 50 p. m.	0	2.5		0	0		3	7	26
Shorey	0		1		8		5	8	4
8 05 p. m.	16,000	1			4		2	8	5
8 33 p. m.	18,000	1.5			3.5		3	6	4
9 44 p. m.	3,000		1.5		3.5		5	6	4
Leopold	0	2			1.5	0	0	6	54
8 07 p. m.	16,000	0.5			4		1	7	60+
8 30 p. m.	18,000	1			5		2	9	54
10 01 p. m.	0	2		0	0	1		14	42
La Motte	0	1		1		3		4	50
7 45 p. m.	16,000	3.5		6			2	4	64
8 45 p. m.	18,000	7		6			2	-2	30
10 03 p. m.	0	2.5		5			2	8	59
Steele	0	2			5	0	0	6	16
8 02 p. m.	16,000	1			4		1	6	18
8 33 p. m.	18,000	6			2		1	3	17
9 53 p. m.	0	3			1		1	5	15
Wheeler	0	0	0		1.5		2	10	10
8 00 p. m.	16,000	1			4		2	8	13
8 20 p. m., given oxygen									
9 47 p. m.	0	1			2		2	8	7
Corneal	0	7			1	1		2	16
7 51 p. m.	16,000	4.5		0	0	1		0	16
8 41 p. m.	18,000	9			4	Unreliable		-4	Unreliable
9 50 p. m.	0	2		0	0	1		4	25

present at ground level, i. e., if the subject had an exophoria to start with it became greater with anoxia, and similarly esophoria increased.

The experiments reported here were made in the low pressure chamber of the Medical School of the University of Pennsylvania through the courtesy of, and with the able assistance of, Dr. Martin Larrabee.

Eight normal subjects had their muscle balance for far and near measured by the Maddox rod and phoropter and for near again with the Maddox wing test. Their involuntary fixation

7 Velhagen, K., Jr. Heterophorie unter den Bedingungen des Hohenfluges, Luftfahrtmedizin 1 344, 1937.

8 Wilmer, W. H., and Berens, C., Jr. V. The Effect of Altitude on Ocular Functions. J. A. M. A. 71 1397 (Oct. 26) 1918.

Technician of the University of Pennsylvania Hospital.)

As soon as the initial measurements were made at ground level the pressure in the chamber was reduced to that corresponding to 16,000 feet (see flight schedule) and the measurements were repeated.

This was done again at 18,000 feet. The descent was then made to ground level, and the measurements were again repeated. During the flight only the observers wore oxygen masks. The experimental subjects showed all the signs of fairly severe anoxia toward the end of the run. One subject had to be given oxygen at 18,000 feet.

Table 1 gives the data of all the tests save those of fusional amplitude. In the first column

is the name of the subject and the time at which his readings were taken, at various altitudes, which are given in the next column. The figures in the following columns are prism diopters, and are self explanatory.

In every case but 1 (Leopold) there was a change in the phoria for distance in the direction of esophoria, regardless of whether the subject

TABLE 2—*Fusion Tests on Orthoptoscope (Grade III Shades)*

Name	Altitude, Feet	Abduction		Adduction	
		Recovery Point		Recovery Point	
Crandall	0	- 8	- 4	+50	+28
	16,000	- 8	- 2	+56	+28
	18,000	0	+10	+58	+34
	0	- 5	0	+50	+34
Mayock	0	- 5	- 3	+26	+11
	16,000	- 2	0	+28	+18
	18,000	+ 2	+ 8	+32	+20
	0	- 2	+ 2	+32	+18
Leopold	0	- 4	- 1	+50	+21
	16,000	- 8	0	+52	+24
	18,000	- 4	+ 4	+50	+22
	0	- 8	+ 4	+64	+32
Shorey	0	- 9	- 6	+16	+11
	16,000	- 4	+ 2	+30	+14
	18,000	- 1	+ 6	+ 6	+ 4
	0	- 7	- 3	+14	+10
Steele	0	- 5	- 3	+45	+15
	16,000	- 2	+ 4	+30	+20
	18,000	+ 4	+ 4	+40	+12
	0	- 4	0	+26	+15
Wheeler	0	- 3	0	+26	+13
	16,000	- 8	0	+30	+10
	18,000	0	- 2	+30	+10
	0	- 4	- 2	+30	+10
Corneal	0	+ 7	+15	+31	+17
	16,000	+ 6	+14	+28	+12
	18,000	0	0	+30	+11
	0	- 1	0	+30	+11
La Motte	0	- 1	+ 9	+60	+39
	16,000	- 2	+20	+66	+53
	18,000	- 2	+20	+60	+48
	0	- 2	+ 4	+80	+50

was esophoric or exophoric to start with. In this exception it will be noticed that the subject was exposed the shortest period of time to the 18,000 foot level. (Compare time table of flight with time of his examination at 18,000 feet. The 18,000 foot level was reached at 8 26 p m and Leopold was tested at 8 30 p m. He had been exposed to this level for only four minutes.) Corneal and La Motte, who were esophoric to start with, became esotropic.

The changes in phoria at 33 cm were not so striking or so constant. The same results were obtained with the Maddox wing test as with the Maddox rod for near. Some of the subjects became more esophoric (or less exophoric) and some did just the reverse. The involuntary vergences showed a lessening of divergence and some increase in convergence. These tests were difficult to carry out in the severely anoxic subjects, and although they point in the same direction as the fusional tests they are not so reliable.

Table 2 gives the results of the tests for fusion done on an orthoscope. From this table the range of fusion was obtained. The figures for this appear in table 3.

In the interpretation of these results certain factors should be taken into account. These are as follows:

1 Familiarity with the test tends to increase the fusion range. Therefore no significance should be attached to the difference between the figures before and after the flight.

2 Convergence tends to increase with repetition.

3 The effect of voluntary effort is less in abduction and at a minimum in abduction-recovery.

4 The fusion range between the breaking points is larger than between the recovery points because stimuli of identical images involuntarily keep the eyes associated as the images

TABLE 3—*Range of Fusion on Orthoptoscope (Grade III Shades)*

Name	Altitude, Feet	Breaking Points	Recovery Points
Crandall	0	- 8 to +50	- 4 to +28
	16,000	- 8 to +56	- 2 to +28
	18,000	0 to +58	+10 to +34
	0	- 5 to +50	0 to +30
Mayock	0	- 5 to +26	- 3 to +11
	16,000	- 2 to +28	0 to +18
	18,000	+ 2 to +32	+ 8 to +20
	0	- 2 to +32	+ 2 to +18
Leopold	0	- 4 to +50	- 1 to +21
	16,000	- 8 to +52	0 to +24
	18,000	- 4 to +50	+ 4 to +22
	0	- 8 to +64	+ 4 to +32
Shorey	0	- 9 to +16	- 6 to +11
	16,000	- 4 to +30	+ 2 to +14
	18,000	- 1 to + 6	+ 6 to + 4
	0	- 7 to +14	+ 3 to +10
Steele	0	- 5 to +45	- 3 to +15
	16,000	- 2 to +30	+ 4 to +20
	18,000	+ 4 to +40	+ 4 to +12
	0	- 4 to +26	0 to +15
Wheeler	0	- 3 to +26	0 to +13
	16,000	- 8 to +30	0 to +10
	18,000	0	- 2 to +10
	0	- 4 to +30	- 2 to +10
Corneal	0	+ 7 to +31	+15 to +17
	16,000	+ 6 to +28	+14 to +12
	18,000	0	0 to +11
	0	- 1 to +30	0 to +11
La Motte	0	- 1 to +60	+ 9 to +39
	16,000	- 2 to +66	+20 to +53
	18,000	- 2 to +60	+20 to +48
	0	- 2 to +80	+ 4 to +50

are moved in or out. Once they are dissociated fusion does not commence until the eyes are inside the range where fusion is easiest.

5 The range of the recovery points is therefore the most accurate index of true fusional ability.

The tests show that the abduction recovery points in 6' out of 8 persons show a consistent shift toward convergence with anoxia. (The 2 who did not conform were unreliable at 18,000

feet in this and in the other tests) The 6 men showed a return toward the divergent position on restoration of oxygen. Only 1 returned as far as his original measurements.

Convergence increases fairly proportionately to the lessening of the divergence, so that there is little change in the range of fusion.

The fusional convergence tends to remain constant or even increase on return to oxygen. This is attributable to repetition and familiarity with the test. If the range of fusion is abnormally low, as it was in 2 cases, it tends to break entirely with anoxia (Shorey was exophoric  $-6$  to  $+11$ , and at 16,000 feet showed the normal change to  $+2$  to  $+14$ . At 18,000 feet an abduction recovery point was obtained at  $+6$ , but recovery of range of fusion was entirely lacking. Corneal was esophoric  $+15$  to  $+17$  and broke from esophoria to esotropia at 16,000 feet and his recovery fusion range at 16,000 feet was absent. No reliable data could be obtained at 18,000 feet.)

From these data one can conclude that during lack of oxygen there is a shift of the range of fusion toward the convergent position. The range itself shows little change in the normal subject if the range is normal at ground level. If the range is abnormally small to begin with, it may be wiped out altogether, and homonymous diplopia may develop.

The development of esophoria under the influence of alcohol and anoxia is due either to an increase in convergence tone or to a diminution of divergence tone. There is no evidence in the literature or in the data presented here which points strongly to either assumption. Velhagen was forced to conclude that some change must occur in the muscles themselves, but this seems unlikely due to the fact that there is no incomitance or anisophoria. All the evidence points to a change in a supranuclear mechanism.

Alcohol is thought to act by depressing the higher centers, and any apparent stimulation results from the "unrestrained activity of lower centers freed by the depression of higher inhibitory control mechanisms."<sup>9</sup> One may assume, therefore, that the convergence mechanism is normally inhibited by higher centers, which alcohol and anoxia remove. There is a parallel example of this in the case of the pupil. During the third stage of anesthesia due to ether and chloroform, the pupil constricts, and this constriction is supposed to be due to the abolition of cerebral impulses which normally inhibit the

tone of the oculomotor constrictor center, i. e., the Edinger-Westphal nucleus.<sup>10</sup> It has also been claimed that during plane 3 of the third stage of anesthesia the eyes are fixed in the convergent position. These forced movements and changes in posture of the eyeballs under general anesthesia have never been satisfactorily studied, and should give some clue to the behavior of the mechanism under discussion.

The esophoria produced by alcohol and anoxia, which may even become esotropia, may not be the same as that which occurs in early childhood and which leads to comitant squint, but there is enough similarity in the two conditions to study squint from this point of view. Both are caused by some interference with a supranuclear mechanism. The comitance of squint proves that the condition is of supranuclear origin. One must keep in mind the fact that comitance may be lost, however, because of lack of use of a squinting eye, and some squints will be labeled incomitant at first because the squinting (and usually amblyopic) eye fails to turn to the temporal side completely. In these cases patching the good eye will usually break up not only the amblyopia but also the incomitance, and the angle of squint will become the same in all directions of gaze. The diagnosis of incomitance should not be made therefore until every effort has been made to break up this motor inhibition.

Chavasse speaks of true paralytic squint losing its incomitance after there is partial recovery, and becoming comitant, but I do not believe that this ever happens, unless, of course, there is complete recovery from the paralysis, and then the squint will disappear. As long as there is weakness of a muscle there will be incomitance. The recovery of function may be sufficient to enable the muscle to pull the eye out completely, but the sound eye will invariably show overshooting (secondary deviation) in this field of action, and thus betray the paralytic origin of the squint.

#### SUMMARY

The eyes are harnessed together by many reflex sources of tone. The chief source of reflex tone is the visual fixation reflex, which serves to keep the two foveas lined up with the object of regard. The cortical center for this reflex lies in area 17, and possibly areas 18 and 19, of Brodmann, and may be thought of as the motor part at least of a true fusion center. Heterophoria is the position the eyes assume when the visual fixation reflex is broken up. The position the

<sup>9</sup> Goodman, L., and Gilman, A. *The Pharmacological Basis of Therapeutics*, New York, The Macmillan Company, 1941, p. 109.

<sup>10</sup> Goodman and Gilman,<sup>9</sup> p. 41.

eyes then assume is due to the sum of all the other sources of reflex tone. These are all from supranuclear mechanisms.

The primary cause of comitant squint is heterophoria, and comitant squint is a manifest heterophoria. The cause of comitant squint must be sought in the cause of the heterophoria. The cause of accommodational squints is known. Many other convergent comitant squints are not accommodational, and as yet nothing is known of their cause.

Alcohol and anoxia produce an esophoria for distance and a shift in the range of fusion toward convergence, and if severe enough may result in a convergent comitant squint. The nonaccommodational convergent comitant squints of childhood should be considered as similar conditions caused by an excessive convergence tone and should be investigated from this point of view. No claim is made that the two conditions are in any way identical.

# Clinical Notes

## INTERSTITIAL KERATITIS TREATED WITH SUBCONJUNCTIVAL INJECTIONS OF PENICILLIN

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The following case of interstitial keratitis is of interest because the progress of the disease was apparently checked by the use of subconjunctival injections of penicillin. No report has been found in the literature of the treatment of interstitial keratitis with subconjunctival injections of penicillin. General antisyphilitic therapy did not seem indicated because the patient had received adequate general treatment for syphilis prior to the beginning of the keratitis. The corneal infiltration and vascularization progressed rapidly until subconjunctival injections of penicillin were used.

### REPORT OF A CASE

Mr. A. F., aged 27, was first seen on Nov. 22, 1944, at which time he stated that his left eye had felt irritated for the past several days. Later, he admitted that he had had a positive Wassermann reaction in 1935 and that his mother's Wassermann reaction was also positive. At that time he had received antisyphilitic treatment, and in 1941 he received another course of therapy. During the past year he received intensive antisyphilitic treatment for four months, while in the army. His Wassermann reaction was still positive, with a titer of 63, and the right upper central incisor was pegged.

Vision was 20/15—1 in the right eye and 20/20—1 in the left eye. The right eye was quiet and appeared normal. There was some ciliary injection of the left eye, with deep infiltration of the cornea above. Dense vascularization had already begun.

On examination with the slit lamp, the right eye appeared normal except for a few pigment stars, which

were considered to be congenital, on the anterior capsule. There was deep infiltration on the upper part of the left cornea, extending almost to the pupillary area, with dense vascularization above. Ophthalmoscopic examination showed the fundi to be normal and the media clear except for interstitial keratitis in the left eye.

The following treatment was prescribed: atropine sulfate, 1 per cent, twice a day, and yellow mercuric oxide ointment, 1 per cent, twice a day, with massage.

The patient was seen six days later, the infiltration and vascularization had extended well into the pupillary area. Vision was reduced to 20/66. From November 29 to December 6, he was given seven subconjunctival injections of 0.5 cc. of sodium penicillin (1,000 Oxford units of penicillin per cubic centimeter). The injections were given above the cornea, at a point corresponding to the area of vascularization. On the fourth day there was less vascularization. On the eighth day the vascularization appeared about the same as at the last examination.

When the patient was seen on December 21, on the twenty-third day after the first subconjunctival injection of penicillin had been given, the eye appeared quiet, with no ciliary injection. The vascularization was subsiding, and the cornea was clearer.

When he was next seen, on Jan. 11, 1945, on the forty-fourth day, the eye was quiet. The vascularization had completely cleared, but there were some scattered areas of deep infiltration of the cornea.

He was last seen Feb. 15, 1945, three months after the onset of his symptoms. His eye was quiet. There were a few faint opacities scattered over the cornea. Vision was 20/15, his eye otherwise appeared normal.



# Ophthalmologic Reviews

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## OPHTHALMODYNAMOMETRY

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The physiology of the vascular circulation in the human eye is of fundamental importance to the whole of ophthalmology, and, because the behavior of the normal and abnormal phenomena are observable within limits, certain analogies, rightly or wrongly, have been drawn with regard to vascular physiology and its alterations elsewhere in the body. Ophthalmodynamometry, a subject of peculiar interest to many workers in this field, appears to deserve review sequential to 1926, when Duke-Elder<sup>1</sup> so aptly observed

The unwieldy literature that has accumulated upon the subject is swollen with wearisomely protracted and often acrimonious discussions of unnecessary hypotheses, with defective and confused experiments based on unsound physiological reasoning, with a multitude of theorizings and a paucity of facts

### REVIEW OF LITERATURE

*Vascular Pulsations*—The basic modifying factor of intraocular pressure has been responsible during approximately two generations for the continuing controversy with regard to the essential principles involved, ever since pulsations of the retinal vessels first were observed ophthalmoscopically in the living human eye by Coccius,<sup>2</sup> in 1853. He noted the existence of a venous pulse, as did van Trigt<sup>3</sup> independently in the same year. Duke-Elder,<sup>1</sup> in discussing the occurrence of the venous pulse and the variations of its amplitude, expressed the belief that its incidence and excursiveness are appreciably influenced by the ease of egress of the venous blood and that this is so because pulsation implies the displacement of fluid

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1 Duke-Elder, W S. *The Ocular Circulation: Its Normal Pressure Relationships and Their Physiological Significance*, Brit J Ophth **10** 513-572 (Oct) 1926

2 Coccius, E A. *Ueber die Anwendung des Augen-Spiegels nebst Angabe eines neuen Instrumentes*, Leipzig, I Müller, 1853

3 van Trigt, A C. *Der Augenspiegel, seine Anwendung und Modificationen, nebst Beiträgen zur Diagnostik innerer Augenkrankheiten*, Lahr, J H Geiger, 1854

Turk<sup>4</sup> demonstrated that the circulatory system in the eye reacts to variations in pressure more after the manner of a series of rigid tubes than does the circulatory system elsewhere. He stated the belief that this was due largely to the influence of the incompressible ocular contents enclosed under pressure or tension by the partially elastic sclera. Duke-Elder<sup>5</sup> demonstrated experimentally that the intraocular tension is limitedly influenced by the height of the general arterial pressure. The former represents a tissue pressure of 20 to 25 mm of mercury (Friedenwald,<sup>6</sup> Duke-Elder<sup>7</sup>), rather than the pressure of 1 to 2 mm of mercury that has been shown to exist elsewhere in the body.

No absolutely accurate method of determining capillary pressure in the eye has been developed but, with the use of a micropipet, Duke-Elder<sup>1</sup> found experimentally that the pressure in the retinal venous capillaries is approximately 2 mm of mercury higher than the tissue pressure (intraocular tension) of the eye. He estimated that the pressure in the arteriolar limbs of the retinal capillaries normally was about 50 to 55 mm of mercury, since he transposed Landis'<sup>8</sup> measurements of pressure in the skin to arrive at a comparable pressure in the eye, that is, Landis demonstrated by the use of a micropipet that with wide variations, the average pressure in the arteriolar limb of a capillary in the skin was about 30 mm of mercury. Duke-Elder,<sup>5</sup> in effect, merely added this approximate figure to the combined values of the normal intraocular tension and the retinal venous capillary pressure.

Duke-Elder<sup>1</sup> also has shown that the pressure in the ophthalmic artery is only slightly below the

4 Turk, S. *Untersuchungen über die Entstehung des physiologischen Netzhautvenenpulses*, Arch f Ophth **48** 513-557, 1899

5 Duke-Elder, W S. *Text-Book of Ophthalmology*, St Louis, C V Mosby Company, 1933, vol 1

6 Friedenwald, J S. *The Pathology of the Ocular Changes in Nephritis and Hypertension*, in *The Kidney in Health and Disease*, Philadelphia, Lea & Febiger, 1935, pp 638-664

7 Duke-Elder, footnotes 1 and 5

8 Landis, E M. *Micro-Injection Studies of Capillary Blood Pressure in Human Skin*, Heart **15** 209-228 (May) 1930

level of the systemic, brachial arterial pressure in the normal person but that the former is approximately 25 per cent greater than the arterial pressure entering the eye. The latter varies from 65 to 85 mm of mercury. The gradient of pressure fall from the central retinal artery, however, is somewhat less than that in other organs, since the capillary pressure in the eye is higher, barring the effects of gravity, than it is elsewhere. It is probable that in the eye the greater part of this fall occurs on the arterial side of the capillary bed, and, as this author pointed out, considerations with regard to the dialysate origin of the aqueous fluid suggest that it does so.

There always exists a pulse in all of the arterial vessels of the body, and this extends down the arterial system with progressively decreasing amplitude. The pulse in the intraocular arterial channels apparently does not differ from that elsewhere in the body except that the intraocular pressure mechanically alters it. The latter varies directly with the blood pressure in the capillaries, and the penetration into the capillary circulation of the variations of the systemic pressure is determined by the height of the general arterial pressure. Complete obliteration of the arteries in the eye may occur at diastole if the diastolic pressure, at the moment, is less than the intraocular pressure. The veins will be full in the eye thus under observation and, therefore, under a pressure higher than that of the intraocular pressure. The capillary pressure must be still higher than the venous pressure, however, since circulatory activity continues indefinitely, thus, capillary pressure may become higher than the diastolic pressure within the entering arteries. Duke-Elder<sup>9</sup> stated, however, that "in normal circumstances the capillary pressure is less than the diastolic, but it need not be, it often is not."

The occurrence of a pulse in the retinal artery first was noted by von Jäger<sup>9</sup> in 1854, but that a spontaneous pulse occurs in the retinas of normal eyes first was observed by Donders<sup>10</sup> in 1855, shortly after the introduction of the ophthalmoscope. Becker,<sup>11</sup> in 1872, expressed agreement with Donders' findings, and Ballantyne,<sup>12</sup> in 1913, estimated that it will be encountered in

approximately 36 per cent of all normal persons and that it may be accompanied with movement of the retinal arterial vessels themselves. The amplitude of the pulse, especially in the branches of the larger vessels, usually may be observed only with special methods because normally it is so small. De Speyr,<sup>13</sup> in 1914, however, demonstrated that physiologic excursions of the pulse too slight to be seen with the standard ophthalmoscope could be observed almost constantly in normal persons with the Gullstrand ophthalmoscope. This observation was confirmed by Kummell<sup>14</sup> in 1915. Galezowski,<sup>15</sup> in 1916, noted the occurrence of an arterial pulse in the choroid, and Onishi,<sup>16</sup> in 1913, expressed his opinion that it could be discerned entoptoscopically in the capillaries. This was confirmed by Scheerer<sup>17</sup> and Fortin<sup>18</sup> independently. Fortin,<sup>18</sup> Bailliart,<sup>19</sup> Fritz<sup>20</sup> and others stated the belief that capillary entoptoscopic phenomena and their proper interpretation are important diagnostic aids in the clinical differentiation of the various forms and stages of local and diffuse vascular diseases. This has yet to receive widespread confirmation.

The degree of excursiveness, or amplitude, of the observable pulsations of the retinal arterial vessels varies considerably both in normal and in disease states. Friedenwald<sup>21</sup> suggested that the pulsations be reconsidered from the standpoint of retinal vascular dynamics with regard to their causation and appearance. He offered the following classification: (1) serpentine, (2) expansile, (3) collapsing and (4) tonic. The first is distinguishable as a movement characterized by a slight shifting of the arterial channel with each cardiac pulse. The displacement may be lateral, or there may be some slight bending or knuckling

13 de Speyr, T. Le pouls des artères rétiniennes. Phénomène physiologique, *Ann d'ocul* **152** 419-429 (Dec) 1914.

14 Kummell, R. Ueber Pulserscheinungen der Augengefäße, *Arch f Augenh* **78** 336-358, 1915.

15 Galezowski, J, cited by Duke-Elder<sup>1</sup>

16 Onishi, Y. Ein Fall von solitartuberkelverdachtiger Veränderung des Augenhintergrundes, *Nippon Gankwa Gakukwai Zasshi* **18** 320-334, 1913.

17 Scheerer, R. Die entoptische Sichtbarkeit der Blutbewegung im Auge und ihre klinische Bedeutung, *Klin Monatsbl f Augenh* **38** 67-107, 1924.

18 Fortin, E. P. Vision directe dans son propre œil des globules du sang et leurs mouvements, applications à l'étude de l'artériosclérose, de l'insuffisance aortique du glaucome et des troubles capillaires, *Semana méd* **2** 126-129 (July 16) 1925.

19 Bailliart, P. L'hypertension artérielle rétinienne, *Internat Cong Ophth* (1937) **1** 87-142, 1938.

20 Fritz, M. Rapport des pressions sanguines humérales et rétiniennes, *Bull Soc belge d'opht* **67** 67-75, 1933.

21 Friedenwald, J. S. Retinal Vascular Dynamics, *Am. J Ophth* **17** 387-395 (May) 1934.

9 von Jäger, E. Ueber die sichtliche Blutbewegung im menschlichen Auge, *Wien med Wchnschr* **4** 36 and 69, 1854.

10 Donders, F. C. Ueber die sichtbaren Erscheinungen der Blutbewegung im Auge, *Arch f Ophth* **1** 75-105, 1854-1855.

11 Becker, O. Ueber die sichtbaren Erscheinungen der Blutbewegung in der menschlichen Netzhaut, *Arch f Ophth* **18** 206-296, 1872.

12 Ballantyne, A. J. Pulsation of the Retinal Arteries, *Ophthalmoscope* **11** 271-285 (May) 1913.

of the vessel. The arterial channel may enlarge during systole and decrease in caliber during diastole, this type he termed expansile. Almost complete emptying during the diastolic shrinkage was termed collapsing. There occasionally are observed in some instances of pregnancy and, of arteriolar sclerosis the halting, slow progression down the vessels of a ring or zone of relative constriction, these movements were called tonic.

The incompressible ocular contents communicate the pressure pulse to the elastic sclera, where it becomes a volume pulse. The latter normally is not grossly visible except when it is magnified by the lever of the tonometer. It is accentuated when the distensibility of the sclera pathologically becomes increased. This field of investigation has been reviewed elsewhere (Duke-Elder<sup>1</sup>).

*Vascular Manometry*—It is known that the normally small retinal arterial pulsations will become progressively larger when the intraocular pressure is raised.<sup>5</sup> Thus, the eye may be converted into a natural sphygmomanometer by the application of the same familiar principles that are involved in the clinical measurement of the systemic arterial blood pressure with the use of the commonplace Riva-Rocci<sup>22</sup> apparatus. This pulse may be artificially induced and become grossly visible in the normal person by the application of gently increased pressure on the globe. The younger the person, the more extensive is the pulsation produced and the less is the pressure required.

The amplitude of this visible pulse increases as the intraocular pressure is increased, until the arteries are seen to be completely collapsed during a portion of the cardiac cycle, at which point the pulsation is maximal. A continued increase of the intraocular pressure will cause the amplitude of this pulsation to decrease progressively, until the incoming blood flow ceases. The systolic pressure is overcome at this point, with cessation of the pulse and collapse of the arterial vessels. The vessels, in the absence of structural changes, will not be visible under the latter conditions because not only are the walls of the retinal vessels normally transparent but there will now exist a transient tissue anemia. Duke-Elder<sup>5</sup> stated: "The point of maximum pulsation therefore records the diastolic of cessation of pulsation the systolic pressure."

The application of pressure, whether positive (Baillart<sup>19</sup> and his followers) or negative (Kukán,<sup>23</sup> Linksz<sup>24</sup>), to the external surface of

the globe produces an increase in intraocular pressure, and, the contents of the eye being incompressible, the lumen of the retinal vessels tends to diminish in diameter. The intraocular pressure, under certain artificial or pathologic conditions, may become equal to that of the diastolic blood pressure within the vessels, and the two pressures will neutralize each other. The vessels at this time, then, contain blood under no pressure, and patency is maintained by the structure of their walls. The walls thus being completely relaxed, a maximum distention normally is presented to the oncoming systemic pulse wave, and a correspondingly large excursion of the pulse ensues.

The firmness of the wall of the retinal artery is overcome when the intraocular tension is increased beyond the retinal diastolic pressure. The pulse wave then must expend a portion of its energy in overcoming the increased intraocular pressure on the compressed arterial wall, with the result that the excursions of the pulse wave within this portion of the vessel are less extensive in proportion to the excess of pressure on the outside of the wall of that vessel. The retinal vessels normally sustain an internal pressure approximately equal to that sustained by vessels of a similar order of size elsewhere in the body, but the pressure in the terminal arterioles most probably is somewhat higher than the average elsewhere. The intraocular pressure however, of approximately 20 mm of mercury, exerts an external supportive force on the intraocular vessels. Friedenwald<sup>6</sup> stated:

It is perhaps as a response to this relief from internal strain that the unusual delicacy of the retinal arterial wall is to be understood. This delicacy of structure may explain the unusually great local effects of changes in blood pressure if these local effects are truly disproportionate to those in other organs and not merely more easily recognizable.

The diastolic blood pressure in the central artery of the retina and in its arteriolar branches normally is greater than the intraocular pressure. An arterial pulsation of varying degree is observed with certain systemic and intraocular conditions, such as aortic insufficiency, hyperthyroidism, impending syncope, severe anemias and glaucoma.<sup>25</sup> The pulsation appears due to the tendency toward equalization of the intraocular

22 Riva-Rocci, S. Un nuovo sfigmomanometro, Gazz med di Torino 47 981, 1891.

23 Kukán, F. Ergebnisse der Blutdruckmessungen mit einem neuen Ophthalmodynamometer, Ztschr f Augenh 90 166-191 (Oct) 1936.

24 Linksz, A. Improved Model of the Kukan Ophthalmodynamometer, Am J. Ophth 25 705-713 (June) 1942.

25 (a) Baillart, P. The Retinal Circulation in the Normal and Pathologic State, translated by J. E. Lebensohn, Chicago, Professional Press, Inc., 1928, (b) footnote 19. (c) Espildora-Luque, C. L'hyper-tension arterielle retinienne solitaire, Internat Cong Ophth (1937) 2 156-182, 1938. (d) Duke-Elder<sup>5</sup>.

pressure and the retinal diastolic blood pressure, for example, in cases of aortic insufficiency with regurgitation the latter undergoes a relative reduction, whereas in cases of glaucoma the former increases

It is possible to elevate the intraocular pressure by instrumentation, by means of manometry or of ophthalmodynamometry.<sup>1</sup> Duke-Elder<sup>5</sup> stated the belief that the former method yields the only reliable values, Baillart<sup>19</sup> remains the chief exponent of the latter, which Terson termed tonoscopy and Magitot called sphygmocopy.<sup>26</sup>

Duke-Elder<sup>1</sup> devised an apparatus by means of which saline solution is forced into the eye after a manometer has been inserted. The pulsatory

pressure in the intact eye is elevated by forcible pressure applied externally to that eye while the vascular pulsatory movements are observed ophthalmoscopically. Von Graefe,<sup>28</sup> in 1854, first correlated this vascular activity with alterations in the intraocular and the systemic arterial pressure. He elaborated his thesis in the following year, however, von Schultén,<sup>29</sup> in 1884, was the first to measure the pressure in the central artery of the retina (table 1). He employed dogs as subjects and attempted to correlate his recorded vascular pressures with the deduced and observed reductions in caliber of the retinal vessels brought about by external pressure on the globe.

Bajardi,<sup>30</sup> in 1906, devised a tonometric type of instrument with which he could measure units of

TABLE 1—Normal Retinal Arterial Blood Pressures Determined with Methods Other Than That of Baillart

Year	Author	Method	Interpreted as Millimeters of Mercury	
			Diastolic	Systolic
1881	Weiss, O. <i>Ztschr f Augenh</i> 25:114, 1881	Manometry (laboratory animal)	50-70	80-100
1884	von Schultén <sup>29</sup>	Manometry, tonometry (laboratory animal, central artery of retina)		90-100
1906	Bajardi <sup>30</sup>	Ophthalmodynamometry (Bajardi)	?	?
1911	Rubino <sup>33</sup>	Ophthalmodynamometry (Bajardi)	49-59	58-67
1914	Henderson <sup>44</sup>	Ophthalmodynamometry (Henderson)	10-25*	
1917	Baillart <sup>27a</sup>	Entoptosecopy	40	69
1923	Smith <sup>41</sup>	Manometry (laboratory animal)	40-50	70-90
1924	Seidel, E. <i>Ber u d Versamml d deutsch ophth Gesellsch</i> 44:79-86, 1924	Manometry (anterior ciliary artery)	30-45	55-75
1924	Bliedung <sup>31</sup>	Ophthalmodynamometry (Bliedung)	55-98	98-165
1924	Lullies, H., and Gulkowitseh, L., edited by Kukán <sup>23</sup>	Manometry (laboratory animal)	54-70	91-108
1926	Duke Elder <sup>1</sup>	Manometry (laboratory animal)	59-69	83-94
1927	Baurmann, M. <i>Arch f Augenh</i> 118:118-130, 1927	Entoptosecopy	40-68	
1930	Baurmann <sup>48</sup>	Ophthalmodynamometry (Baurmann)	36	
1934	Spinelli <sup>49</sup>	Ophthalmodynamometry (Spinelli)	36-48	
1934	Uyemura and Suganuma <sup>50</sup>	Ophthalmodynamometry (Uyemura and Suganuma)	30-4	56-5
1936	Suganuma <sup>52</sup>	Ophthalmodynamometry (Uyemura and Suganuma)	30-6-54-8	50-2-85-5
1936	Sobánski <sup>47</sup>	Ophthalmodynamometry (Sobánski)	45	75
1936	Kukán <sup>23</sup>	Ophthalmodynamometry (Kukán)	42-3	
1937	Kell <sup>51</sup>	Ophthalmodynamometry (Kell)	35-40	65-75
1937	Müller, Bruning and Sohr <sup>46</sup>	Ophthalmodynamometry (Baillart, Sobánski and Uyemura and Suganuma), eyes of cadavers in situ	36-48	
1941	Linksz <sup>53</sup>	Ophthalmodynamometry (Linksz)	39-46-5	65-75
1943	Gutmann <sup>52</sup>	Ophthalmodynamometry (Gutmann), rabbits	40-3-49-5	59-62-1

\* Values for tonometric readings must be added to these figures in individual cases

behavior of the retinal vessels thus can be observed microscopically by the excursions of an air bubble in a capillary tube, and this activity is correlated with the volume pulse of the globe, its amplitude and the points of maximum oscillation and the cessation of oscillation of the arterial pulse. This method is not adapted to practical clinical use.

The second method, that of Baillart,<sup>27</sup> is a procedure by means of which the intraocular

26 Baillart, P. Ophthalmodynamometry, in Ridley, F., and Sorsby, A. *Modern Trends in Ophthalmology*, London, Butterworth & Co., Ltd., 1940, pp 195-199.

27 Baillart, P. (a) *Circulation arterielle retinienne. Essais de détermination de la tension arterielle dans les branches de l'artere centrale de la retine*, *Ann d'ocul* 154:257-271, 1917, (b) *La circulation retinienne a l'état normal et à l'état pathologique. Procédés modernes d'examen et de diagnostic*. Paris, Gaston Doin, 1923.

pressure applied to the external surface of the living human eye. No records of the figures he obtained are available, although Bliedung<sup>31</sup> and Cattaneo<sup>32</sup> referred to them. Rubino,<sup>33</sup> in 1911,

28 von Graefe, A. *Notiz über die Pulsphanomene auf der Netzhaut*, *Arch f Ophth* 1(pt 1):382-390, 1854.

29 von Schultén, M. W. *Experimentelle Untersuchungen über die Circulationsverhältnisse des Auges*, *Arch f Ophth* 30(pt 3):1-76, 1884.

30 Bajardi, G., cited by Rubino<sup>33</sup>

31 Bliedung, C. *Die Beziehungen zwischen allgemeinem Blutdruck, Blutdruck in den intraokularen Gefassen und Augendruck*, *Arch f Augenh* 94:198-257, 1924.

32 Cattaneo, D. *PAR (Pressione dell'arteria centrale della retina) e alterazioni retiniche nelle encefalopatie a focolare da disturbi circolatori*, *Internat Cong Ophth* (1937) 2:112-119, 1938.

33 Rubino, C. *La pressione del sangue nell'arteria retinica e suoi rapporti con la pressione nel circolo del Willis*, *Riforma med* 27:1345-1353 (Dec 4) 1911.

published the values obtained by him with the Bajardi apparatus Henderson,<sup>34</sup> in 1914, devised a small, ingenious hand apparatus for the measurement or estimation of retinal arterial pulsation. He utilized a Geneva lens measure graduated, apparently more or less arbitrarily, in millimeters of mercury, instead of in diopters. The pointed foot plate was replaced with a small knob. He expressed the belief that his instrument would register in millimeters of mercury the pressure which when exerted on the globe through the eyelid was sufficient to bring about the appearance of the diastolic pulsation. Magitot<sup>35</sup> stated that the value for the intraocular pressure was added to the figure obtained for the diastolic retinal blood pressure, Henderson's original communication, however, makes no mention of specific values for intraocular pressure other than to state that the retinal diastolic blood pressure ranged in children from 10 to 15 mm of mercury higher than the intraocular tension and in adults from 15 to 25 mm higher.

Baillart<sup>36</sup> previously, in 1909, had observed that rather strong digital pressure on the globe was required to bring about the disappearance (systolic pressure) of the retinal arterial pulse in patients with elevated systemic blood pressure. He stated the belief that this was of clinical significance. Black,<sup>37</sup> in 1911 and Deyl,<sup>38</sup> in 1912, confirmed this observation and tended to agree with the derived conclusions.

Baillart,<sup>39</sup> in 1917, recalling Marey's "law" of the inverse relationship between heart rate and arterial pressure, and employing the mechanical principles of the Bloch-Verdin<sup>40</sup> sphygmomanometer, devised a standardized tension spring instrument for applying and registering increasing

pressures on the living human eye. Priestly Smith<sup>41</sup> stated that Baillart had no previous knowledge of Henderson's apparatus. A Schiøtz tonometer (old model) then was used to determine the intraocular tensions (or pressures) for correlation with the retinal diastolic and systolic blood pressures obtained. Baillart termed the apparatus an ophthalmodynamometer, and two types were manufactured. Each essentially is a cylinder arrangement, but one model has etched on the piston or rod a column of horizontal graduated markings. The rod slides upward and downward within the cylinder or sleeve of the instrument and works against a spring. The other model possesses a dial with radial markings on its periphery. A pointer which is activated by the movements of the piston within the metal sleeve is directed to these markings, a second pointer registers the highest reading obtained. Both instruments are calibrated to measure retinal diastolic and systolic blood pressures ranging from 10 to 150 Gm of water in units of 10.

Pressure may be made on the eye with an ophthalmodynamometer during an ophthalmoscopic examination after local anesthetization has been induced. The retinal blood pressure values obtained may be read from the scale incorporated in the instrument, although it is necessary to convert these figures into units of millimeters of mercury, when the intraocular tension is known for comparison and correlation with the systemic brachial blood pressures. The conversion graph of Magitot and Baillart,<sup>42</sup> which is based on values obtained from studies on cat eyes, is used for this purpose with this instrument. Duke-Elder<sup>1</sup> has pointed out that the method of Baillart involves several fallacies in principle and that it is not the pressure in the branches of the central artery of the retina, but the pressure in the ophthalmic artery, that is obtained. The maintenance of a uniform pressure normally without subjective fluctuations in the ophthalmic artery, is believed to be effected because of the very appreciable reduction in caliber of the internal carotid artery immediately distal to the branching off of the ophthalmic artery.<sup>21</sup>

Numerous workers have recorded their observations with the ophthalmodynamometer of Baillart, while many of the values are relatively low, some of the figures vary from others by more than 100 per cent. There also are recorded

34 Henderson, T. Clinical Proof of the Venous Level of the Intra-Ocular Pressure and a Method of Estimating the Arterial Diastolic Pressure in the Eye and Its Clinical Significance, *Tr Ophth Soc U Kingdom* 34 309-315, 1914.

35 Magitot, A. P. How to Know the Blood Pressure in the Vessels of the Retina, *Am J Ophth* 5 777-784 (Oct) 1922.

36 Baillart, P. Contribution a l'etude du pouls retinien, *Clin opht* 15 178-183, 1909.

37 Black, M. An Index to the General Blood Pressure. The Venous Pulse and Blanching of the Retinal Vessels Induced by Pressure on the Eyeball, *J A M A* 57 362-363 (July 29) 1911.

38 Deyl, A. Retinale Angiosklerose als differential diagnostisches Symptom, *Wien klin Wchnschr* 26 33-51, 1912.

39 Baillart, P. (a) La pression arterielle dans les branches de l'artere centrale de la retine, nouvelle technique pour la determiner, *Ann d'ocul* 154 648-666, 1917, (b) footnote 27<sup>a</sup>.

40 Bloch, A. M. Note sur un perfectionnement apporte a mon sphygmometre, *Compt rend Soc de biol* 48 745-746 (July) 1896.

41 Smith, P. The Blood Pressure in the Eye and Its Relation to Chamber Pressure, *Brit J Ophth* 7 449-469 (Oct) 1923.

42 Magitot, A. P., and Baillart, P. Modifications de la tension oculaire sous l'influence de pressions exercees sur le globe (recherches experimentales), *Ann d'ocul* 156 656-666, 1919.



variations in figures obtained on different occasions by the same authors using the same technic. Thus Bailliant<sup>39a</sup> in 1917 obtained average values of 25 to 30 and 50 to 70 mm of mercury for the normal retinal diastolic and systolic blood pressures, respectively, in man, and Magitot and Bailliant<sup>43</sup> in 1921 determined the normal range in man to be 30 to 35 and 70 to 80 mm of mercury for these two blood pressures. The same authors in 1919 had obtained values as high as 100 to 130 mm of mercury for the retinal diastolic blood pressure in the cat and in the dog, respectively.<sup>42</sup> Bliedung,<sup>31</sup> as well as Fritz,<sup>20</sup> and Constantine<sup>44</sup> have recorded the widest range of values for the retinal systolic blood pressure. Bliedung,<sup>31</sup> who used his own device also found the widest range of recorded retinal diastolic blood pressures. Workers recording narrow ranges (table 2) are in the majority, however, although less striking variations, with the exception of those just mentioned, exist with regard to the figures obtained by workers with methods other than the technic of Bailliant (table 1). It is of interest to note that Lebensohn<sup>45</sup> who in 1925 was the first in this country to record his observations with the ophthalmodynamometer of Bailliant, obtained readings that closely approximate those of most other workers.

Constantine,<sup>44</sup> in her study of the interrelationship of retinal and systemic arterial blood pressures and tonometric pressure in normal and in syphilitic patients, stated "The method [of Bailliant] is palpably inaccurate and open to wide differences, depending on the personal equation of the observer." Bailliant felt that certain errors could be eliminated to some extent by furnishing both types of his instrument with a convex rather than a concave foot plate, since if it were equipped with the latter the examiner would have difficulty in ascertaining whether or not a portion of the edge of the foot plate or the whole of the concave disk was exerting pressure on the sclera. He expressed the opinion that some possible errors, therefore, would be decreased if only a convex surface were permitted for application to the eye. This view has been disputed by the findings of Muller, Bruning and Sohr,<sup>46</sup>

who, using their reduction scale (or conversion graph) reading in millimeters of mercury, rather than in grams of water, and working on the human eye and the cat's eye, found no differences in the values obtained with the apparatus of Bailliant<sup>27a</sup> and that of Sobánski.<sup>47</sup> The latter has a concave foot plate.

TABLE 2—Retinal Arterial Blood Pressures in Normal Persons Determined with Ophthalmodynamometric Method of Bailliant

Year	Author	Interpreted as Millimeters of Mercury	
		Diastolic	Systolic
1917	Bailliant <sup>27a</sup>	67	98
1917	Bailliant <sup>39a</sup>	25-30	50-70
1920	Velter, E. Arch d'ophth 37: 88-94, 1920	35	60-65
1920	Duverger, C. and Barré, J. A. Arch d'ophth 37: 71-87, 1920	50-60	80-100
1921	Magitot and Bailliant <sup>43</sup>	30-35	70-80
1921	Vossius, A. Arch f Ophth 104: 330-324, 1921		70
1921	Gaudissart, P. Am J Ophth 4: 500-503 (July) 1921	30-35	70-80
1922	Salvati, G. Ann d'ocul 159: 69-71, 1922	32-50	60-70
1925	Stasinski, J. Klin oczna 3: 49-58, 1925	30-35	67-70
1925	Lebensohn <sup>45</sup>	30-35	65-75
1925	Vita, A. Ann di ottal e clin oculi 53: 904-913, 1925	30-35	70-75
1925	Verway, A. South African M Rec 23: 427-429, 1925	Equals radial pressure	
1925	Monjukova, N. and Pleitnera, N. Arch oftal 1: 212-242, 1925	35	70
1926	Baurmann, M. Klin Monatsbl f Augenh 41: 874, 1926	49-75	54-9
1926	Rasvan, N. Bull Soc roumaine d'ophth, 1926 pp 201-205	30-35	65-70
1926	Lida, E. and Adroque, E. Compt rend Soc de biol 95: 1160-1161, 1926	40-50	80-100
1926	Samojloff, A. J. Ann d'ocul 163: 689-694 (Sept) 1926	35	80-85
1927	Schiötz, L. Acta ophth 5: 293-297, 1927	50-56	70-80
1927	Abramowicz, I. Klin oczna 5: 125-173, 1927	45-55	70-90
1927	Kalt, M. Pression arterielle retinienne dans l'hypertension intracranienne. Paris, L'expansion scientifique, 1927	35	77
1927	Serr, M. Arch f Ophth 119: 6-14, 1927	30-35	50-70
1928	Berens, Smith and Cornwall <sup>64</sup>	18-48	36-88
1931	Vancea, P. Arch f Ophth 126: 601-612, 1931	25-42	55-77
1932	Guiral <sup>61</sup>	30-35	70-80
1933	Fritz <sup>20</sup>	25-45	60-130
1936	Sobánski, J. Arch f Ophth 135: 372-430, 1936	40-56	68-88
1937	Bailliant <sup>19</sup>	30-35	50-80
1937	Bengisu <sup>55</sup>	23-55	
1939	Constantine <sup>44</sup>	22-72	65-112
1941	Koch <sup>56</sup>	20-41	

\* Includes value of 20 mm of mercury for normal tonometric readings.

Aside from the more recent modifications and the newer, ingenious ophthalmodynamometric instruments of Baurmann,<sup>48</sup> Spinelli,<sup>49</sup> Uyemura

bánski am menschlichen Leichenaugen, Internat Cong Ophth (1937) 4: 44-51, 1938

47 Sobánski, J. Ein Ophthalmodynamometer und seine Handhabung. Klin Monatsbl f Augenh 96: 351-356 (March) 1936

48 Baurmann, M. Ein neues Dynamometer, Arch f Ophth 124: 693-704, (Aug) 1930

49 Spinelli, F. Angiotensimetro retinico. Spinelli, Atti d Cong Soc ital oftal (1934), 1935 pp 795-798

43 Magitot, A. P. and Bailliant, P. Recherches sur l'action de vasomoteurs oculaires. Pression comparée dans les vaisseaux de l'iris et de la rétine, J de physiol et de path gén 19: 532-541, 1921

44 Constantine, E. F. A Study of the Interrelationship of Retinal and Systemic Arterial Pressure and Intra-Ocular Tension in Normal and Syphilitic Patients, Am J Ophth 23: 436-445 (April) 1940

45 Lebensohn, J. E. The Determination of Retinal Blood Pressure, Illinois M J 48: 212-214 (Sept.) 1925

46 Müller, H. K., Brüning, A., and Sohr, H. Die Eichung der Dynamometer von Bailliant und So-



and Sukanuma,<sup>50</sup> Sobanski,<sup>47</sup> Kukan,<sup>23</sup> Keil,<sup>51</sup> Linksz,<sup>24</sup> Gutmann<sup>52</sup> and others, the method and the apparatus used by the majority of the workers in this field have been those of Baillart (table 2). The published reports of the latter are concerned largely with the clinically diagnostic significance of the blood pressures in the central artery of the retina as measured in its ophthalmoscopically visible branches on the papilla in normal persons and in patients who have diffuse vascular disease with systemic hypertension, whether or not of renal origin.

Duke-Elder<sup>1</sup> determined in the cat with manometric methods that the mean pressure in the ophthalmic artery is about 95 per cent and that in the retinal arterioles about 70 per cent of the mean aortic pressure. Baillart,<sup>27b</sup> in 1923, with ophthalmodynamometric methods, estimated that the diastolic pressure in the retinal arterioles was about 45 per cent of the diastolic pressure in the brachial arteries of the normal adult.

Magitot and Baillart<sup>42</sup> previously had found, in 1919, that in eyes with normal intraocular tension a dynamometric pressure of approximately 25 Gm of water was required to produce the retinal arterial pulse and that 60 to 70 Gm of water was sufficient pressure to cause its disappearance. Thus, the retinal diastolic blood pressure in normal persons was believed to be 30 to 35 mm of mercury, while the retinal systolic blood pressure, according to their conversion graph (reduction scale), was 65 to 70 mm of mercury. The figure for the diastolic pressure was the more constant, and it was found that a factor, 0.45, could be utilized to predict the retinal diastolic blood pressure if the systemic brachial diastolic blood pressure was known. Multiplying the systemic pressure by this factor yielded a theoretic ideal, or normal, value for the retinal diastolic blood pressure.

A similar but not quite so consistent a constant was offered in the factor 0.54, which when multiplied by the value of the known systemic brachial systolic blood pressure, was believed to yield the value for the normal retinal systolic blood pressure. Baillart<sup>25a</sup> stated it as his opinion that the latter, at least, was of practical clinical importance in that he deemed it unwise to exert a pressure of more than 150 Gm of water on the eye, since this represented a pressure

less than would be employed by the patient in pressing on his own eye. This pressure is well below that required to produce an oculocardiac reflex. He expressed the belief, too, that the constants, or factors just mentioned, had a further clinical application, since their use could detect deviations from the theoretic normal and not infrequently could be relied on in instances in which it was not feasible to use his apparatus. Thus, if these derived values are greater than 5 to 10 mm of mercury, there may, he stated, be said to exist a truly disproportionate or abnormal reciprocal relationship between the systemic and the intraocular blood pressure system.

Retinal vascular hypertension and hypotension, Baillart and his followers<sup>53</sup> asserted, may be diagnostic in very early phases of alteration in the systemic blood pressure, as well as of clinical value when the change in the retinal pressure exists in the "solitary" state. The latter, for example, refers to the existence of a disproportionate reciprocal relationship encountered by these workers in cases of increased intracranial pressure without systemic hypertension, that is, they found the retinal blood pressures to be elevated. They stated, too, that there may occur prodromal retinal hypertension without any change in the ophthalmoscopic findings or in the systemic blood pressure, and they asserted that these circumstances constitute an aid in the diagnosis of diffuse arterial disease with hypertension.

There now exists an extensive literature with regard to the ophthalmodynamometric investigations of ocular and systemic pathologic states in which variations in the retinal blood pressures and in the intraocular tension have been suspected. Many of the published figures, as has been indicated, are inconclusive and controversial, accordingly, no unanimity of interpretation exists. Wagener and Keith,<sup>54</sup> however, in their comprehensive review of diffuse arteriolar disease with hypertension, probably expressed the consensus in the statement

53 (a) Baillart, P., Magniel, and Saragea. Mesures de la pression arterielle retinienne et de la tension cephalo-rachidienne dans quelques cas d'hypertension arterielle, *Arch d mal du coeur* **17** 289-294 (May) 1924. (b) Baillart<sup>19</sup>. (c) Espildora-Luque<sup>25c</sup>. (d) D'Osvaldo, E. Sull'importanza clinica del segno di Baillart come indice di ipertensione arteriose cefalica (Espildora), *Lettura oftal* **10** 455-466 (Oct) 1933. (e) Sukanuma, S. Studien über den Blutdruck in der Zentralarterie der Netzhaut II. Ueber den Blutdruck in der Zentralarterie der Netzhaut bei verschiedenen Formen von allgemeiner Hypertonie und über die sog isolierte zephale Hypertension, *Klin Monatsbl f Augenh* **97** 498-514 (Oct) 1936.

54 Wagener, H. P., and Keith, N. M. Diffuse Arteriolar Disease with Hypertension and the Associated Retinal Lesions, *Medicine* **18** 317-430 (Sept) 1939.

50 Uyemura, M., and Sukanuma, S. Ueber einen neuen Ophthalmodynamometer, *Acta Soc ophth jap* **38** 1835-1844, 1934.

51 Keil, J. Ein neues Ophthalmodynamometer, *Klin Monatsbl f Augenh* **99** 625-636 (Dec) 1937.

52 Gutmann, A. Pressure in Central Artery of Retina in Allergy with Description of a New Ophthalmodynamometer, *Arch Ophth* **29** 457-460 (March) 1943.

The pressures as measured by this method may be lower than the actual figures, but they furnish a ready and probably fairly reliable method of determining variations from the normal in pathologic states

My own investigations tend only partially to confirm this point of view.<sup>55</sup>

#### CLINICAL EVALUATION

It is impossible accurately to evaluate for clinical comparison the results obtained with the ophthalmodynamometer by many of the workers in this field not only because dissimilar instruments and technics have been employed but because the majority of the investigators (as has been true, also, in the study of vascular micrometry) have not troubled sufficiently to correlate the values obtained with reference to classification of the disease groups studied, age subgroupings, systemic blood pressures, ophthalmoscopic findings and other diagnostic minutiae. It appears, too, that not infrequently there has been inadequate comprehension of vascular physiology in general. Conclusions have been derived in many instances in which there was little recognition of the existence of errors in measurements due, most unfortunately, to the intangible factor inherent in the personal equation necessarily present on the part of the observer in any clinical examination. Tuyl,<sup>56</sup> in particular, stated that only comparative values, at best, are obtainable with the ophthalmodynamometric technic and that long experience and numerous readings in every case are necessary in order to arrive at acceptable values. It is of interest that the proponents of vascular dynamometry enthusiastically believe it elicits clinical information of at least somewhat, if not appreciably, greater value than any other single test or procedure for the recognition and differential diagnosis of many abnormal and pathologic states, of either general or local ocular origin.

Despite the many contributions in the field of ocular dynamometry, there are tremendous variations in the values obtained for normal retinal blood pressures no matter with what instrument the examinations were conducted (tables 1 and 2). It is impossible to denote any single exact value for either the diastolic or the systolic blood pressure, although many workers have concluded that there must be some such figure. It appears unreasonable, therefore, to suppose that any single value for the retinal blood pressures can be given when it is known that no single value can be cited with reference to the systemic blood

pressures no matter in what location or with what apparatus they are determined.

The values for the normal retinal diastolic blood pressure, obtained through more than two decades of investigation with the ophthalmodynamometer of Baillart, range from a low of 18 to a high of 72 mm of mercury, and there is some overlapping with the values for the retinal systolic pressure, since the range for the latter is 36 to 130 mm of mercury (table 2). Similar variations in the range of retinal blood pressures have been obtained when instruments and methods other than Baillart's have been employed, however, the ranges with manometric devices although not clinically practical, generally have been narrower than when some form of the dynamometer has been used (table 1).

Retinal capillary pressures also have been studied by several workers, whose contributions have been reviewed by Kukán,<sup>23</sup> Fortin,<sup>18</sup> Baillart,<sup>19</sup> Fritz,<sup>20</sup> Baratta<sup>57</sup> and others tended to attribute greater physiologic importance than had heretofore been thought necessary to the role played by these smaller vascular channels in systemic hypertensive disease, as well as in states of altered intracranial and intraocular function. Numerous objective and subjective procedures have been devised or suggested whereby the physiologic and the abnormally physiologic status of these vessels might be employed as clinical aids, particularly in cases of hypertensive disease. None appear to be satisfactory.

In general, ophthalmodynamometric values for retinal diastolic blood pressures, in millimeters of mercury, probably must be considered normal if the value obtained does not exceed 55.<sup>55</sup> The lower limit of normal is similarly variable and somewhat more difficult to determine. Bengisu<sup>58</sup> probably represents the consensus in his values for the normal retinal diastolic blood pressure obtained with the dynamometer of Baillart. His examinations indicated that approximately 10 per cent of normal persons will have a retinal diastolic blood pressure of 23 to 25 mm of mercury, that a second group, representing 45 per cent of normal persons, will have values ranging from 35 to 45 mm and that a third, more elderly, group, of 45 per cent of normal persons, will

57 Baratta, O. Studio sulla circolazione vascolare della retina con particolare riguardo al comportamento della pressione dell'arteria centrale (PAR) e dei capillari della macula (PCR) nelle affezioni renali, *Ateneo parmense* 9 265-295 (July-Aug.) 1937.

55 Koch, F. L. P. Retina in Systemic Vascular Hypertension. A Clinical Study of the Caliber of the Retinal Arterioles and the Retinal Arterial Diastolic Blood Pressure, *Arch Ophth* 26 565-581 (Oct.) 1941.

56 Tuyl, A., in discussion on Espildora-Luque<sup>25c</sup>

58 Bengisu, N., in discussion on Lobeck, E. Ueber die ophthalmoskopische Messung der Durchmesser der Netzhautgefasse und ihre allgemein klinische Bedeutung fur die Differentialdiagnose bei Hochdruck- und Nierenkrankheiten, *Internat Cong Ophth* (1937) 2 262-164, 1938.

have values of from 50 to 55 mm of mercury Linksz,<sup>59</sup> with his negative pressure dynamometer, found slightly higher values 39 mm of mercury for persons from 15 to 30 years of age, 44.5 mm for persons from 30 to 50 years of age and 46.5 mm for persons from 50 to 70 years of age. My own figures, obtained with the Bailliant device, were somewhat lower.<sup>55</sup>

I found that my values, when expressed, as seems clinically rational, in terms of the percentage ratio of retinal to brachial diastolic blood pressure, ranged from 25 to 51, with means of 36, 40 and 43 per cent for the normal patients in three major age subgroupings, respectively, of 8 to 15, 16 to 40 and 41 to 60 years, however, there was considerable overlapping from one individual to another. There existed a progressive increase in the retinal diastolic blood pressure and in the percentage ratio of the retinal diastolic to the brachial diastolic blood pressure in hypertensive groups. This was less manifest in the patients with chronic glomerulonephritis. The study indicated, however, that a mean percentage ratio that was considered normal, of 55, as has been mentioned, arbitrarily could be established as the upper limit of normal and that, although there was some overlapping of the ratios for patients with mild hypertension in the younger age group with the ratios for normal persons in all age groups and with those for patients with chronic glomerulonephritis, this overlapping was in accord with the fluctuation in systemic blood pressures that is known to exist normally.<sup>55</sup>

Most of the workers with the Bailliant ophthalmodynamometer have stated, however, that it is difficult to fix an exact value for the minimal or theoretically normal diastolic retinal blood pressure unless the figure for the systemic diastolic blood pressure is multiplied by the factor 0.45. This figure was stated originally by Bailliant to represent the percentage ratio of the normal retinal to the normal systemic diastolic blood pressure. Bailliant<sup>60</sup> expressed the opinion that a comparison of this derived figure with the actual value obtained by the ophthalmodynamometric examination is of diagnostic value when there is a variation of more than 5 to 10 mm of mercury and that there exists, therefore, a local retinal or cephalic ("solitary") vascular hypertension which a general examination will reveal to be systemic or cerebral in origin. The values obtained in my studies with reference to the theoretic, or derived, as compared with the actual

retinal diastolic blood pressures, expressed in millimeters of mercury, and their relationship to the percentage ratios of the retinal and the systemic diastolic pressures indicate that there exist relatively normal values for the nonhypertensive patients but that elevated, abnormal, relatively disproportionate values are found for the hypertensive groups.<sup>55</sup>

Bailliant, Magniel and Saragea<sup>58a</sup> found somewhat similar progressively increasing values for 22 hypertensive patients. These patients were not specifically classified as to the stage of the disease. The systemic diastolic blood pressures in this group ranged from 50 to 180 mm of mercury, while the retinal diastolic blood pressures ranged from 20 to 120 mm. The percentage ratios varied from 33 to 96, while the spinal fluid pressures ranged from 75 to 320 mm of water. Guiral,<sup>61</sup> Fritz<sup>20</sup> and other followers of Bailliant generally expressed agreement with these conclusions. In general, a rise in the estimated retinal diastolic blood pressure, in millimeters of mercury, is only roughly proportionate to the rise in brachial diastolic blood pressure. The mean percentage ratio, while it increases as the hypertensive disease becomes advanced, exhibits only a rather narrow range of values from the normal subjects to group 4 (malignant hypertension), however, this ratio is almost directly proportional to that obtained by multiplying the mean brachial diastolic blood pressure for each group of patients by the factor 0.45.

The dynamometer of Uyemura and Suganuma,<sup>60</sup> instead of registering values by means of spring tension, as do most others, depends on hydrostatic pressure. Suganuma<sup>62</sup> measured the retinal diastolic pressure in a single eye, usually the right, of 65 patients with normal blood pressure. These patients ranged in age from 12 to 65 years. Their retinal diastolic blood pressures ranged from 30.6 to 54.8 mm, while the brachial diastolic blood pressure ranged from 42 to 87 mm, of mercury. Intraocular tension with the old model Schiøtz tonometer ranged from 8 to 22 mm of mercury. Suganuma also obtained dynamometric readings for both eyes of 18 patients, who ranged in age from 16 to 30 years. They were unselected normal persons of both sexes. The mean retinal diastolic blood pressure was 38.08 mm of mercury, on a basis of values

61 Guiral, R. J. La disociacion tensional retino-humeral, *Arch de neuro-biol* 12: 275-294 (May-June) 1932.

62 Suganuma, S. Studien über den Blutdruck in der Zentralarterie der Netzhaut. I. Ueber den Blutdruck in der Zentralarterie der Netzhaut bei gesunden Menschen und über seine Beziehung zum allgemeinen Blutdruck, *Klin Monatsbl f Augenh* 96: 74-84 (Jan) 1936.

59 Linksz, A. A New Instrument for Ophthalmodynamometry, read at the meeting of the New York Society for Clinical Ophthalmology, Nov. 3, 1941.

60 Bailliant (footnotes 25<sup>a</sup> and 27<sup>b</sup>).

ranging from 30.6 to 45.2 mm of mercury. Since he obtained a mean value of 31 mm from the readings on single eyes in a similar, but larger, group, the significance of this difference in values is uncertain (table 3).

An analysis of the values obtained by Suganuma was made with reference to age subgroups, systemic and retinal vascular pressures, the ratio of these pressures in percentages and the theoretic mean ratio obtained by means of the factor, 0.45, of Baillart. These data are summarized in table 3, in general, it was found that his values for the retinal diastolic blood pressure in normal persons from 8 to 65 years of age are higher than those obtained in my study.<sup>65</sup> The

TABLE 3—Analysis of Values Obtained by Suganuma<sup>62</sup> in Normal Persons

Age in Years, Inclusive	Number of Subjects	Mean		Theoretic Ratio (Baillart)
		Diastolic Blood Pressures, Mm	Ratio of Retinal to Brachial Blood Pressure, Per Cent	
8-15	2 (2 eyes)	57	40	70
16-40	55 (53 eyes)	69	38	55
41-60	7 (7 eyes)	65	43	65
Mean all persons		69	39	56

percentage ratios necessarily are rather higher, too, because of his relatively lower figures for the brachial diastolic blood pressure. This low pressure also results in a somewhat lower theoretic, or ideal, retinal diastolic blood pressure.

Muller, Bruning and Sohr<sup>46</sup> evolved comparative curves for use with the dynamometers of Baillart, Sobánski and Uyemura and Suganuma. They determined the mean retinal diastolic blood pressure to be 48 mm of mercury for 180 eyes of 98 persons who probably had been healthy prior to death. These eyes were examined in situ in cadavers a few to twenty-four hours after death in each instance. The Franck manometer was used in conjunction with their investigations. They came to the conclusion that the conversion graph curves of Sobánski and of Baillart were essentially similar and could be used more or less interchangeably but that attempts to convert the values obtained with the Uyemura-Suganuma instrument in terms of the conversion graphs of the previously mentioned authors would result in a mean value of 60 mm of mercury for the "normal" retinal diastolic blood pressure. It will be recalled that Duke-Elder,<sup>5</sup> with manometric methods, found that the retinal diastolic blood pressure ranged from 59 to 69 mm of mercury.

It is interesting to compare the mean values for local ocular and systemic pressures obtained

for normal persons by Bliedung,<sup>11</sup> in 1924, by means of a cambric bandage and a hydrostatic device in conjunction with ocular manometry. His figures (table 4) are all very high for the 350 eyes of the 292 patients examined. Their ages ranged from 9 to 67 years, inclusive. The intraocular tension averaged 20 mm of mercury for the entire group, but the retinal diastolic blood pressures, arterial and arteriolar, were nearly equal to and greater than, respectively, the brachial diastolic blood pressure, expressed in millimeters of mercury. There was a slight increase in the retinal pressures in the older age groups as compared with those in the younger subgroups. Bliedung's values have not been accepted by other workers in this field.

Suganuma,<sup>63</sup> using the dynamometer bearing his and Uyemura's name, determined the ophthalmodynamometric relationships with reference to the systemic blood pressures in normally pregnant women and in women with toxemia of pregnancy. He also obtained what he believed were diagnostic values for patients with hypertensive disease and for patients with "solitary," cephalic hypertension.<sup>58e</sup> This investigator obtained what he considered were normal values in

TABLE 4—Intraocular Pressures in Normal Persons (Bliedung<sup>11</sup>)

Age Groups, Years	Number of Subjects	Number of Eyes	Mean			
			Brachial Diastolic Pressure, Mm Hg	Retinal Diastolic Pressure in Central Artery, Mm Hg	Diastolic Blood Pressure in Retinal Arteries, Mm Hg	Intraocular Pressure (Schlötz-Tonometer, Old Model), Mm
9-15	48	60	63	64	77	22
16-20	48	60	69	71	78	21
21-25	41	50	75	70	81	20
26-35	41	50	69	63	83	21
36-45	14	50	73	70	83	20
46-55	43	50	78	74	87	18
56-67	27	30	84	75	91	18
9-67	292	350	69	69	82	20

normally pregnant women both before and after delivery, however, he studied only 10 patients, 1 of whom he was unable to observe after delivery (table 5). His values for the retinal diastolic blood pressure in this group of patients essentially are the same as those in the normal groups analyzed in table 3. This is true, also, with respect to the systemic diastolic pressures, the percentage ratios and the values for the latter.

63 Suganuma, S. Studien über den Blutdruck in der Zentralarterie der Netzhaut. III. Ueber den Blutdruck in der Netzhautarterie während des Verlaufes der normalen Schwangerschaft und der Schwangerschaftstoxikose, sowie über seine frühdiagnostische Bedeutung. Klin Monatsbl f Augenh 99: 637-654 (Nov) 1937.

obtained by means of the Baillart factor of 0.45. The percentage drop in the brachial diastolic pressure from the value preceding delivery to that following delivery was nearly twice as great as the percentage drop in the retinal diastolic blood pressure, the values being 17 and 10 per cent, respectively.

Suganuma obtained definitely higher, but essentially proportional, values in a similar study on

TABLE 5—Analysis of Values Obtained by Suganuma<sup>63</sup> for Normally Pregnant Women

Values for Ten Patients							
Age	Before Delivery			After Delivery			
	Arterial Blood Pressures, Mm of Hg		Intra ocular Tension, Mm of Hg	Arterial Blood Pressures, Mm of Hg		Intra ocular Tension, Mm of Hg	
	Systemic	Retinal		Systemic	Retinal		
27	117/78 114/74	56 5/36 5 58 0/39 4	18 17	114/68	56 4/36 2	19	
26	112/58 104/60	59 6/34 0 59 6/36 0	15 16	106/48	58 4/36 0	17	
24	120/58	62 6/49 0	15	114/68	59 0/40 2	17	
23	112/72	64 2/39 2	15	118/76	63 2/41 8	12	
24	112/64	62 6/31 6	13	106/62	59 0/31 2	15	
26	89/50 96/55	48 0/36 2 51 6/34 8	10 9				
22	112/72	69 4/44 1	13	118/68	58 6/33 8	15	
27	118/68 120/70	58 3/38 6 70 6/48 8	15 15	116/68	60 4/39 8	17	
40	140/96	85 8/54 6	15	124/62	63 1/40 6	15	
23	104/48 108/54	62 5/39 4 72 4/50 2	15 15	108/56	56 5/36 4	17	
Analysis of Mean Values							
				Theoretic Ratio (Bailhart) of Retinal to Systemic Diastolic Blood Pressure, Multiplied by 0.45			
Before delivery			76.95	41.05	53.36	34.63	
After delivery			64.00	37.33	58.34	28.80	
Decrease in per cent			17	10			

10 patients presenting various stages of hypertensive toxemia of pregnancy (table 6). It should be noted, however, that the percentage drop from the value preceding delivery to that following delivery was essentially the same in this toxemic group with reference both to their brachial and to their retinal diastolic blood pressures. This is in accord with the findings of Baillart.<sup>25a</sup>

Suganuma's<sup>53e</sup> studies with respect to other forms of elevation of systemic pressure are summarized in tables 7, 8 and 9. There exists no truly appreciable difference between the values for his various groups of hypertensive patients and the values for various age subgroupings. This is true with respect to all the values obtained and is particularly striking when the mean values for each particular group of hypertensive patients

are examined. It also will be observed that the highest recorded mean brachial diastolic blood pressure in his Japanese patients was 116 mm of mercury. This is of interest, although of doubtful significance, when it is noted that the mean retinal diastolic blood pressures, as well as the percentage ratios, in all these groups generally are as high as, if not higher than, the values for the patients with similar brachial diastolic blood pressures examined in my investigation.<sup>55</sup> The group of patients with toxemia of pregnancy observed by Suganuma had retinal diastolic blood pressures and percentage ratios that approached the lower values obtained in his groups of hypertensive patients.

Baillart,<sup>26</sup> in his earlier work, as well as later, stated that retinal hypertension might exist inde-

TABLE 6—Analysis of Values Obtained by Suganuma<sup>62</sup> for Women with Toxemias of Pregnancy

Age	Values for Ten Patients					
	Before Delivery			After Delivery		
	Arterial Blood Pressures, Mm. of Hg		Intra ocular Tension, Mm. of Hg	Arterial Blood Pressures, Mm. of Hg		Intra ocular Tension, Mm. of Hg
	Systemic	Retinal		Systemic	Retinal	
21	104/ 80 138/103	88 0/64 0	15	114/ 78 148/ 98 142/ 86 104/ 74	84 2/59 8 58 6/33 8	17 17
24	182/102	87 0/65 7	13	118/ 68	60 4/37 6	18
29	130/ 92	80 0/64 2	11	116/ 70	62 1/41 8	13
29	166/103	80 6/65 5	17			
22	110/ 56	60 2/42 8 75 4/53 8				
33	166/104 195/134	86 8/62 8	16	168/112 138/ 95	84 0/62 6 79 0/55 7	15 14
30	118/ 76	76 0/48 7	11	122/ 80	85 6/62 2	17
34	186/120	122 7/88 0	21	132/ 88	113 0/84 7	19
25	180/110	82 0/57 1	17	152/ 98	78 5/50 1	19
35				200/112	109 0/78 2	

Analysis of Mean Values				Theoretic Ratio (Bailliant)
			Ratio of Retinal to Systemic Diastolic Blood Pressure, Per Cent	Retinal to Systemic Diastolic Blood Pressure Multiplied by 0.45
	Diastolic Blood Pressures, Mm			
	Systemic	Retinal		
Before delivery	95.88	62.15	64.78	43.15
After delivery	87.25	57.15	65.60	39.26
Decrease in per cent	9	8		

pendently of systemic hypertension and that, since the circulation in the retina reflects generally that of the brain, the existence of retinal hypertension thus implies the coexistence of cerebral hypertension, probably largely on the basis of an increased intracranial pressure, whether brought about by local intracranial or by systemic hypertension. Conversely, hypotension also may be encountered. His observations have received



support from his followers and from some other investigators

Guiral,<sup>61</sup> among others, stated the belief that if the retinal vascular pressures were elevated in a patient over 50 years of age there existed imminent danger of a cerebral vascular accident, that if the systemic blood pressure was elevated, although the retinal blood pressure remained high, even greater danger was present but that if the retinal and systemic pressures were proportional the prognosis was less grave. Berens, Smith and Cornwall<sup>64</sup> concluded from their studies on 11 normal persons and on 13 patients with neuro-ophthalmologic syndromes that the

TABLE 7—Analysis of Values Obtained by Suganuma<sup>53c</sup> for Patients with Essential Hypertension

Age in Years, Inclusive	Number of Patients	Mean		Ratio of Retinal to Brachial Blood Pressure, Per Cent
		Diastolic Blood Pressures, Mm		
		Brachial	Retinal	
29-39	5 (5 eyes)	109	77	70
41-60	35 (35 eyes)	106	72	68
(5 patients 61 to 74)				
Mean	All patients	107	73	68

method of Baillart is of value to the trained observer in spite of its inaccuracies but that the use of the ophthalmoscope nevertheless is invaluable. They also stated the opinion that the retinal diastolic blood pressure increases rather markedly as the subject changes from a standing or sitting to a prone position. This view is not altogether in accord with the findings of others, although both Salvati<sup>65</sup> and de Sanctis<sup>66</sup> supported it.

It was the opinion expressed by these authors and by others, particularly Klar,<sup>67</sup> Espildora-Luque<sup>25c</sup> and de Morsier, Monnier and Streiff,<sup>68</sup> that the retinal arterial pressure becomes elevated in the presence of intracranial disturbances, particularly lesions of the posterior fossa, such as

64 Berens, C., Smith, H. T., and Cornwall, L. H. Changes in the Fundus and in the Blood Pressure in the Retinal Arteries in Increased Intracranial Pressure, *Arch Neurol & Psychiat* 20 1151-1171 (Dec) 1928

65 Salvati, G. La tension oculaire en position assise et couchee, *Ann d'ocul* 159-128-130, 1922

66 de Sanctis, R. Il comportamento della P A R (Pressione arteriosa retinica) nelle diverse posizioni del corpo, *Internat Cong Ophth* (1937) 2 119-137, 1938

67 Klar, J. Hypertonia arterialis retinae post commotionem cerebri, *Internat Cong Ophth* (1937) 2-52-56, 1938

68 de Morsier, G., Monnier, M., and Streiff, E. B. La tension artérielle rétinienne dans les tumeurs intracrâniennes, *Rev neurol* 71-702-714 (June) 1939

neoplasms, trauma and cerebrovascular accidents. The last-mentioned authors asserted that retinal arterial hypertension, nevertheless, is relatively infrequent with tumors, but they agreed with Klar that it is very common as a sequel of cerebral trauma. These workers said that it probably develops subsequent to disturbances of the regulatory centers of the cerebral vasomotor system.

Espildora-Luque,<sup>25c</sup> d'Oswaldo,<sup>53d</sup> Cattaneo,<sup>3-</sup> Suganuma<sup>53e</sup> and others examined relatively small groups of patients and concluded that so-called solitary hypertension is present with rather a large number of diseases, both systemic and local, which affect both intracranial and intra-ocular pressure relationships. Espildora-Luque<sup>25c</sup> has proposed, and Suganuma<sup>53e</sup> is in accord with the suggestion, that this occurrence be termed cephalic arterial hypertension, since it is thought that this rise of retinal vascular pressure occurs in the absence of elevation of systemic blood pressure but in the presence of increased cerebrospinal fluid pressure. These authors and others, on the basis of what appears to be insufficient evidence, stated that this increase of local vascular pressure is coincident with, and secondary to, an increase in blood pressure which is limited to the region of the internal carotid arteries and the circle of Willis and its branches. It is more logical to assume that this increase in local pressure, if it occurs (as seems evident),

TABLE 8—Analysis of Values Obtained by Suganuma<sup>53e</sup> for Patients with Primary Contracted Kidney

Age in Years, Inclusive	Number of Patients	Mean		Ratio of Retinal to Brachial Blood Pressure, Per Cent
		Diastolic Blood Pressures, Mm		
		Brachial	Retinal	
41-60 (1 patient of 61)	3 (3 eyes)	111	81	73

probably is secondary to the rise of the cerebrospinal fluid, as noted by Pickering<sup>69</sup> in cases of this type. Conversely, however, this does not necessarily imply that a rather low retinal diastolic blood pressure value is accompanied with a decrease in pressure of the cerebrospinal fluid, nor, if the latter is normal, can it be inferred that the former is normal or low.

D'Oswaldo<sup>53d</sup> stated the opinion that the systemic vascular hypertension which later appeared in 3 of 10 patients with solitary cephalic hypertension, whom he previously had examined, already was present clinically, and probably

69 Pickering, G. W. The Cerebrospinal Fluid Pressure in Arterial Hypertension, *Clin Sc* 1 397-413 (Dec 27) 1934



should have been diagnosed as such, at the time of the first examination Espildora-Luque<sup>26c</sup> and others found an elevation of retinal arterial pressures in patients with glaucoma, retrobulbar neuritis, intracranial tumors, meningitis, meningo-encephalitis, cerebral trauma, myopia, optic neuritis, hereditary syphilis and the various forms of hypertensive disease and nephritic disease, all either with or without edema of the optic papilla. He classified this solitary cephalic hypertension into four types cephalic, vertiginous, visual and neurologic, all depending, again, on whether the lesions appear to be intraocular or intracranial.

TABLE 9—Analysis of Values Obtained by Suganuma<sup>53e</sup> for Patients with Chronic Nephritis and with Secondary Contracted Kidney

Age in Years, Inclusive	Number of Patients	Mean Diastolic Blood Pressures, Mm		Ratio of Retinal to Brachial Blood Pressure, Per Cent
		Brachial	Retinal	
16-40	14 (14 eyes)	116	81	70
41-60	13 (13 eyes)	101	65	64
(3 patients 61 to 76)				
Mean	All patients	109	74	68

One wonders if a new category is necessitated by the group of 10 patients with allergy recently reported on by Gutmann<sup>52</sup> as having increased pressure in the central artery of the retina. This author was stimulated by his clinical findings to sensitize 5 rabbits with horse serum after initial ophthalmodynamometric readings were taken with his modified Baillart instrument. He concluded that the later rise in intraocular vascular pressures in the animals was proof of successful sensitization and that the rabbits had become allergic, accordingly, he stated the belief that the higher pressures in the central arteries of his 10 patients were caused by the allergic status of their nasal mucous membranes.

Retinal arterial hypotension and its relation to the systemic arterial pressure and the intraocular tension have been studied in detail by both Lauber<sup>70</sup> and Sobanski.<sup>71</sup> Each stated the belief that there exists a minimum level of retinal diastolic blood pressure below which the capillary circulation functions only poorly. They expressed the opinion that systemic hypotension, particularly diastolic, accompanies progressive tabetic

70 Lauber, H. Der Einfluss niedrigen allgemeinen Blutdruckes auf den Verlauf von Sehnervenerkrankungen, Wien klin Wchnschr 48 1079-1081 (Aug 30) 1935

71 Sobanski, J. Das Wesen der tabischen Sehnerv-  
venatrophie und ihre Behandlung, Arch f Ophth  
135 401-430, 1936

atrophy and that there is a subsequent lowering in the retinal diastolic arterial pressure from the normal range of 40 to 56 mm of mercury, as determined by them. These authors stated that the optic nerve atrophy thus produced is subsequent to local ocular circulatory failure, since it was their belief that the local arterial pressure in this condition tends to decrease toward and below the level of the intraocular tension. Constantine,<sup>44</sup> who reviewed this field in her study of the interrelationship of retinal and systemic pressure in normal persons and in syphilitic patients, not only was unable to confirm either their work or their theories but found that the differential between the retinal diastolic arterial pressure and the intraocular pressure was higher than normal in patients with syphilis of the central nervous system, either with or without optic nerve atrophy. The brachial blood pressures she obtained generally were slightly higher in the latter group than in the normal patients.

Suganuma<sup>53e</sup> examined 36 eyes in 30 patients whose general examinations revealed the existence of asthma, hysteria, nervousness, beriberi, headache, arteriosclerosis and atherosclerosis, dizziness, nasal empyema, epilepsy, chronic nephritis, pregnancy, migraine, optic nerve atrophy, neuroretinitis, both of local and of sys-

TABLE 10—Analysis of Values Obtained by Suganuma<sup>53e</sup> for Patients with Solitary Cephalic Hypertension

Age In Years, Inclusive	No of Pa tients	Mean						Ratio of Retinal to Brachial Blood Pressure, Per Cent
		Blood Pressures, Mm				Sys tolie	Dias tolie	
		Systemic		Retinal				
		Sys tolie	Dias tolie	Sys tolie	Dias tolie			
8 15	1 (1eye)	128	73	82	71	66	97	
16 40	19 (22 eyes)	125	76	82	56	66	74	
41 60 (1 patient of 72)	10 (13 eyes)	131	82	83	57	64	69	
Mean	All patients	127	78	83	56	65	71	

temic origin, acute choroiditis, peripheral neuritis and retrobulbar neuritis. It is not clear whether these clinical diagnoses were arrived at prior to or after the determination of the retinal pressures and their relationships to the other measurements obtained. These values have been analyzed by me in table 10 from the figures given by Suganuma. The significance of the mean values recorded in this table is not clear, although it will be observed that, while the percentage ratios closely approximate those obtained for the patients with systemic hypertension (tables 7, 8 and 9), the retinal diastolic pressures are almost midway in value between those ob-

tained by this author for patients with hypertensive disease and those obtained for normal persons, whereas the brachial diastolic pressures are in accord with the figures accepted as normal for the occidental races. The percentage ratios, however, of the retinal systolic to the brachial systolic pressures are consistently lower, although not notably so, than are those for the diastolic pressures. Suganuma did not comment on this particular point, but throughout all of his studies he appeared to stress the importance of the systolic rather than the diastolic retinal blood pressure. Parenthetically, the great majority of workers in both vascular manometry, or ophthalmodynamometry, and vascular micrometry seems to stress, for reasons not altogether clear, the systolic blood pressures and the arterio-venous ratios respectively, rather than the associated diastolic pressures and the caliber of the arterioles and veins as distinguished from each other.

#### COMMENT

It is unfortunate that the few studies which have been carried out in some detail with reference to the various pressure relationships involved have not followed a relatively standard

procedure with regard both to the ophthalmodynamometric methods and apparatus employed and to the classification of normal and of abnormal states according to uniform criteria of diagnosis. The reports in the available literature, however, with respect to investigations on the various vascular pressure relationships confront the worker in this field with an inescapable sense of the futility of efforts to arrive at any reasonably definite values for the normal retinal blood pressures. It becomes practically impossible therefore to rely diagnostically on the figures given by the various investigators for the retinal blood pressures in the numerous forms or stages of local and systemic hypertensive disease of whatever cause. It would appear to be much more reasonable to depend primarily on the information gained from a careful ophthalmologic examination, with particular reference to all of the changes that manifest themselves in the retinal vessels, particularly the arterioles, and in the retina and choroid as well, and these findings necessarily must be correlated with the results of the general physical examination.

60 East Seventy-Fifth Street

## Correspondence

### KERATITIS DUE TO N-BUTYL ALCOHOL

*To the Editor* —In a recent report (An Unusual Type of Keratitis Associated with the Exposure to N-Butyl Alcohol [Butanol], *ARCH OPTH* 33:106 [Feb] 1945) describing keratitis in 28 workers exposed to n-butyl alcohol (butanol) we overlooked an article by M. Bucklers (Tropfenformige Niederschläge auf der Hornhautoberfläche bei Mobelarbeitern, *Klin Monatsbl f Augenh* 99: 676, 1937) describing what appears to have been the same condition in furniture lacquerers. The causative agent was unknown to Bucklers, since the composition of the lacquer was an industrial secret, but the author's description of vacuoles ("not larger than 40 microns") situated symmetrically in the epithelium of otherwise clear corneas, the occurrence of severe epiphora, burning and watering of the eyes, and the complete reversibility of the process when the patients stayed away from their work leave little doubt that the keratitis which we described in connection with the use of n-butyl alcohol was in fact, the same condition as Bucklers described in furniture workers. We assume, therefore, that the responsible agent in his cases was also n-butyl alcohol.

One of the outstanding differences between Bucklers' conclusions and ours, however, is in the matter of hypersensitivity. Since only a few of the employees in the industrial process with which Bucklers was concerned had complained of ocular irritation, the author assumed that some

idiosyncrasy was necessary to account for the keratitis. In our series, on the other hand, we found that the majority of workers exposed to n-butyl alcohol vapor, including those who had no subjective symptoms, presented the characteristic corneal involvement and that the degree of involvement corresponded approximately to the concentration of the vapor. It did not seem necessary, therefore, to assume that the affected persons were hypersensitive.

NOTE —We should like to take this opportunity of recording further pertinent data obtained since we submitted our first communication. We previously reported our failure to obtain corneal lesions in various animals exposed to n-butyl alcohol vapor. Since, however, butyl acetate was present along with butyl alcohol in connection with the cases reported by E. Kruger (*Augenerkrankungen bei Verwendung von Nitrolacken in der Strohhutindustrie, Arch f Gewerbepath u Gewerbehyg* 3: 798, 1932), we have exposed 6 guinea pigs and 6 albino rabbits to vapors of butyl acetate for varying lengths of time and examined their corneas periodically with the biomicroscope. As in the case of butyl alcohol, the results were negative. No abnormality was found in these animals after continuous exposure for ninety-six hours to 700 parts per million or to 1,100 parts per million nor for two weeks to 350 to 550 parts per million.

DAVID G. COGAN, M.D., and  
W. MORTON GRANT, M.D.

243 Charles Street, Boston

# News and Notes

EDITED BY DR W L BENEDICT

## PERSONAL NEWS

**Leslie Dana Gold Medal Award**—The Leslie Dana Gold Medal, awarded annually for outstanding achievements in the prevention of blindness and the conservation of vision, will be presented this year to Dr William Zentmayer, of Philadelphia, it is announced by the National Society for the Prevention of Blindness, Inc

Dr Zentmayer was selected for this honor by the St Louis Society for the Blind, through which the medal is offered by Mr Leslie Dana, of St Louis. This highly prized token of recognition in the field of public health is given on the recommendation of the Association for Research in Ophthalmology.

Despite his eighty years, Dr Zentmayer is in active practice as an ophthalmologist. He is professor emeritus of diseases of the eye, Graduate School of Medicine, University of Pennsylvania, and consulting surgeon to Wills Hospital, St Mary's Hospital and Glen Mills School, all in Philadelphia. He received his degree of Doctor of Medicine from the University of Pennsylvania School of Medicine in 1886.

Dr Zentmayer is a member of numerous medical, public health and other scientific organizations. He has served as president of the American Ophthalmological Society, chairman of the Section on Ophthalmology, American Medical Association, chairman of the section on ophthalmology, College of Physicians, Philadelphia, editor of the College of Physicians of Philadelphia Transactions and Studies, associate editor, ARCHIVES OF OPHTHALMOLOGY, and chairman of the section on eye, ear, nose and throat, Medical Society of the State of Pennsylvania. He is a member of the board of directors of the National Society for the Prevention of Blindness, Inc.

The conditions of the Leslie Dana Gold Medal award set forth that it is to be made for "long meritorious service in the conservation of vision in the prevention and cure of diseases dangerous to eyesight, research and instruction in ophthalmology and allied subjects, social service for the control of eye diseases, and special discoveries

in the domain of general science or medicine of exceptional importance in conservation of vision."

## GENERAL NEWS

**Graduate Course in Ophthalmology and Otolaryngology, Gill Memorial Eye, Ear and Throat Hospital**—The nineteenth annual spring graduate course in ophthalmology and otolaryngology will be held at the Gill Memorial Eye, Ear and Throat Hospital, Roanoke, Va., April 1 to 16, 1946.

**Second Pan-American Congress of Ophthalmology**—The official meeting place of the Second Pan-American Congress of Ophthalmology, which will take place in Montevideo, Uruguay, Nov 26 to Dec 1, 1945, is the Municipal Hotel, Miramar, on Carrasco Beach. This is a first class, modern hotel, and the city of Montevideo has fixed the reduced rate of \$5 per day for room and meals for congress guests. Inasmuch as all program sessions, the scientific and commercial exhibits and social affairs will take place in that hotel, it will be convenient for congress guests to stay there. Reservations may be made through Dr Conrad Berens, 301 East Fourteenth Street, New York 3. Such requests should include the names of all persons in the party.

Any one who desires to stay in some other hotel should make requests for reservations to the treasurer of the congress, Dr Julio A Sicardi, Agrupación Universitaria, Ave Agracida 1464, P 13, Montevideo, Uruguay.

The registration fee for members of the congress is \$11 United States money (\$20 Uruguayan), and for others in the party who wish to be included in the social events, \$5.50 United States money, per person. These fees may also be paid in advance to Dr Berens.

Because of general travel conditions, it was not possible to make arrangements for persons attending the congress from the United States to go in a group. The Pan-American Airways and the American Express Company will cooperate in doing everything possible to work out transportation plans to meet individual requirements.

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

## Anatomy and Embryology

CONCERNING THE RELATIONS OF THE DEVELOPING OPTIC NERVE TO THE RECESSUS OPTICUS AND THE HYPOPHYSIS IN YOUNG FOETUSES A STUDY OF SEVEN HUMAN FOETUSES 4 MM TO 40 MM, INCLUSIVE H C HADEN, *Am J Opth* 27:1 (Oct, pt 2) 1944

The sixth de Schweinitz Lecture, delivered before the Section on Ophthalmology of the College of Physicians, Philadelphia, appears as a supplement to the October issue of the *American Journal of Ophthalmology*. It contains a number of illustrations but does not lend itself to abstracting

W S REESE

## Conjunctiva

LOCAL PENICILLIN THERAPY IN OPHTHALMIA NEONATORUM SORSBY and E HOFFA, *Brit M J* 1 114 (Jan 27) 1945

The authors state that, unlike the sulfonamide compounds, penicillin remains effective in the presence of pus. It therefore has great possibilities for the local treatment of ophthalmia neonatorum in place of general sulfonamide treatment. Forty-seven infants in the ophthalmia neonatorum unit at White Oak (London County Council) Hospital were treated with penicillin. The concentrations began at 500 Oxford units per cubic centimeter and were gradually increased to 2,500 units, the doses were instilled at half hour intervals for the first three hours, then hourly for twenty-four hours and every two hours thereafter.

In a comparison of penicillin therapy and general sulfonamide treatment, the authors speak of the advantages of local treatment and avoidance of the danger of sensitization. At the same time, frequent irrigations are a trial to the infant and a considerable burden to the nurse. As the concentrations were increased from 500 to 2,500 units, there was an increasing proportion of satisfactory results. The authors conclude that in adequate concentration penicillin appears to be effective against all the common causal organisms of ophthalmia neonatorum, including the virus of inclusion blennorrhea. It is likely that some forms of ophthalmia neonatorum respond more readily to penicillin than others, but on the whole the results are of the same order as those obtained with the sulfonamide compounds.

ARNOLD KNAPP

## Congenital Anomalies

UNUSUAL PRELACRIMAL CONGENITAL MALFORMATION M SORIA ESCUDERO, *Arch Soc de oftal hispano-am* 3 471 (Nov-Dec) 1943

A boy 6 years of age presented a small congenital sinus, about 2 mm deep, in the region of the lacrimal sac, immediately below the canthal ligament. There was no connection with the sac.

The author has been unable to find in the literature any previous report of such a condition.

H F CARRASQUILLO

A CASE OF PERSISTENCE OF THE HYALOID ARTERY INTERESTING ASPECT OF ITS OPHTHALMOŠCOPIC IDENTIFICATION N P DE FIGUEIREDO, *Rev brasil de oftal* 2 121 (March) 1944

De Figueiredo identified the hyaloid artery in the eye of a man 26 years of age. The patient exhibited dental abnormalities of intrauterine origin. The author believes that the persistence of the hyaloid artery depends on a sudden cessation of the involution of the artery during the last few months of intrauterine life due to syphilis, which increases in virulence during the last few months of pregnancy. Syphilis is also the cause of the dental abnormalities which are often associated with persistence of the hyaloid artery.

W ZENTMAYER

## General Diseases

OPHTHALMOLOGIC LESIONS ENCOUNTERED IN TROPICS, WITH SPECIAL REFERENCE TO OCULAR MANIFESTATIONS OF MALARIA J N ROBERTSON, *North Carolina M J* 5:483 (Oct) 1944

According to Robertson, optic neuritis and amblyopia are at times associated with malaria. This form of amblyopia has to be differentiated from that which is due to quinine. In the latter the condition depends on the retinal anemia resulting from the toxic spasm of the arterioles, there are extreme pallor of the optic disks and contraction of the visual fields. This picture is in contrast to the hyperemic disk and retina associated with malarial toxemia. Malarial amblyopia occurs as a result of the action of the malarial toxin on the optic nerve and retina. Often optic neuritis and papillary edema result from the blocking of the retinal and choroidal vessels by parasites and leukocytes. The retinal

hemorrhages are usually small, multiple and peripheral, large macular hemorrhages do occur with the malignant types of malaria. Ulceration of the cornea is the most common ocular sequela of malaria, and recurrent iritis is frequently associated with this keratitis. Supraorbital neuralgia precedes the corneal lesions. Photophobia and lacrimation are characteristic signs and often precede the corneal lesions by days or weeks. On an island in the Southwest Pacific the author encountered many patients with intraocular disturbances among men between the ages of 20 and 30. Many had suffered some depletion of the powers of accommodation and convergence, as was manifested by the complaints of difficulties in reading, scotomas and muscular imbalance, particularly exophorias. Subjectively, the complaints were loss of vision, frequent headaches in the occipital or temporal region, dizziness, pain in the eyeballs, tenderness on palpation, photophobia, lacrimation and spots before the eyes. The objective findings were irregularity of the pupils, retinitis of the atrophic type, usually in or around the macular area, unusual concentration of choroidal pigmentation, generalized hyperemia of the retina and nerve head, optic neuritis, both mild and severe, optic nerve atrophy, and, in a few cases, severe progressive choroidoretinitis and uveitis. Some of the patients who were evacuated were followed up by the author after his return. Some of these men now have chronic uveitis.

J A M A W ZENTMAYER

### General Pathology

**HISTOLOGIC NOTES (A) PRESENCE OF ANOMALOUS FORMS OF CONES IN NORMAL RETINAS (B) DEGENERATIVE LESION IN THE CONES IN A CASE OF OVERDOSE IN THE THERAPEUTIC USE OF ROENTGEN RAYS** A GALLEO FERNANDEZ, Arch Soc oftal hispano-am 4:177 (March-April) 1944

Galleo Fernandez made his observations on the previously normal eye of a man 38 years of age which was enucleated on account of a severe penetrating wound and on an eye which was removed after the incorrect use of roentgen rays in treatment of a carcinoma of the upper lid. In the first eye, using the technic of Balbuena, the author observed that in the region of the macula some cones had their nuclei located immediately above the external limiting membrane, and not below it, as generally occurs. In the other eye, besides all the generalized histologic changes in the ocular tissues, he noted lesions in the retina which up to the present have not been fully studied. Crowding of Nissl granules in the ganglion cells was observed. The nuclear layers showed no change except infiltration with blood cells. The author calls attention to the changes seen in some of the cones. There were thickening

and retraction of the internal filament, and large vacuoles appeared in the foot plates. These changes occurred only in the cones in the region of the macula.

H F CARRASQUILLO

### Glaucoma

**VOGT'S CYCLODIATHERMY PUNCTURES IN TREATMENT OF GLAUCOMA** A PALOMAR PALOMAR, Arch Soc oftal hispano-am 4:608 (July-Aug) 1944

The author discusses in detail this method of treatment for glaucoma. He states that in spite of the gratifying results shown in statistics published up to this time and of his own work it is erroneous to believe that this new method may supplant other operations which are now in continual use. He gives the following indications for this new procedure: (1) hemorrhagic glaucoma, (2) acute glaucoma when medical treatment or basal iridectomy has failed, (3) glaucoma secondary to iridocyclitis when iridectomy has not been successful, (4) painful absolute glaucoma when other procedures have failed, (5) glaucoma associated with aphakia or luxation of the crystalline lens, (6) secondary glaucoma with adherent leukoma, when iridectomy has failed, (7) all forms of glaucoma when the anterior chamber has disappeared, as a primary operation or after some other procedure has failed, (8) chronic simple glaucoma when the visual fields have been much reduced, (9) all forms of glaucoma when other operations have failed or any other intervention is likely to produce total loss of vision.

H F CARRASQUILLO

**HEMICYCLODIALYSIS AND ITS USE IN TREATMENT OF CHRONIC SIMPLE GLAUCOMA** E GRAUE JR, Bol d hosp oftal de Nuestra Señora de la Luz 2:51 (Sept-Dec) 1942

Graue uses what he calls hemicyclocalysis as the operation of choice for simple glaucoma. The operation is a modification of the cyclocalysis procedure of Heine, which, without knowledge of the author, was advocated by Elschnig some years before. It consists in performing a disinsertion of the ciliary muscle in half of the circumference of the limbus according to the technic of Heine. The results after this operation, according to the author, are better than those in any other type of surgical procedure.

H F CARRASQUILLO

### Lacrimal Apparatus

**PSEUDODACRYOCYSTOBLENNORRHEA** M LOPEZ ENRIQUEZ, Arch Soc de oftal hispano-am 3:474 (Nov-Dec) 1943

The author gives this name to a process characterized by anatomicophysiologic integrity of



the lacrimal sac accompanied with persistent lachrimation and a continuous purulent secretion through one of the lacrimal puncta

Two cases are reported. The condition was produced by a fistulous tract, established from a previous chalazion, which opened into the lacrimal sac.

H. F. CARRASQUILLO

**ABORTIVE TREATMENT OF DACRYOCYSTITIS** L. ORTIN, Arch Soc de oftal hispano-am 3:476 (Nov-Dec) 1943

Dacryocystitis may occur as an inflammation of the tear sac itself or as a pericystic process with or without involvement of the sac. The pericystic condition may arise from a previously diseased sac or may be a blood-borne infection with no relation to any pathologic condition of the sac. The canaliculi and the lacrimal duct may or may not be occluded.

Conservative initial treatment may avoid surgical intervention. If the canaliculi are imperious and there is suppuration within the sac, the lumen is opened by injecting under pressure a few drops of a solution containing 5 or 10 per cent cocaine in a 1:1,000 solution of epinephrine hydrochloride. The sac is emptied by pressure and then irrigated with a 3 per cent solution of boric acid, followed by a lotion containing mercury oxycyanide (1:4,000). The same procedure is repeated next day, and then a few drops of 1 or 2 per cent silver nitrate is injected into the sac, followed by irrigation with water if there is retention. If complete obstruction of the canaliculi exists, a no. 1 probe may be used to dilate the opening. If there is inflammation around the sac secondary to infection of the sac, the same treatment is given. However, if pus forms, an incision should be made, but this should not go deep into the cavity of the sac.

H. F. CARRASQUILLO

## Lids

**ALOPECIA AREATA (PELADA) OF THE EYELIDS** H. MARBACK, Arq brasil de oftal 6:211 (Dec) 1943

Marback reports the case of an adolescent boy of 14 years who presented total alopecia areata (pelada) of the left upper eyelid. The eyes showed no other abnormality and functioned normally. The age of the patient at the time the condition appeared was not known. There was no history of local trauma or of the use of any local drug. One of the parents had syphilis. The patient was observed for about two months during which the alopecia was limited to the left upper eyelid. Antisyphilitic therapy, consisting of administration of quinine bismuthodide, was carried out for about three months, in the course of which the eyelashes reappeared and grew normally; they became permanent and were still

present at the time of the report, two years and a half after discontinuation of the therapy.

W. ZENTMAYER

**MARCUS GUNN'S PHENOMENON** J. DE PAULA XAVIER, Arq brasil de oftal 6:213 (Dec) 1943

De Paula Xavier reports the case of a boy 11 years of age who presented the jaw-winking phenomenon on the right side. The syndrome had been present from infancy. The patient was otherwise normal. There was right hyperopia and amblyopia ex anopsia of the right eye. Blepharoptosis was pronounced. The involved eye opened when the patient opened the mouth or made masticatory movements to either side with the mouth either closed or opened, when the chin was projected and when the frontalis muscle was contracted. The Wassermann reaction of the blood was negative. The mother had had two abortions.

Surgical intervention may lessen the blepharoptosis. In some cases the blepharoptosis is decreased by compensatory contraction of the frontalis muscle. Progressive improvement in spontaneous opening of the eye can be expected as the child grows to adult life. Operation is indicated early in adult life if there is still conspicuous blepharoptosis. The patient was instructed in using the frontalis muscle for opening the eye.

W. ZENTMAYER

## Neurology

**LOCALIZATION OF CEREBRAL LESION** P. FALCAO, Arq brasil de oftal 7:1 (Feb) 1944

Falcao directs attention to the value of ocular neurologic symptoms in the diagnosis of the site of a cerebral lesion. A destructive lesion of the optic nerve causes total blindness of the eye. A medial sagittal lesion of the optic chiasm with involvement of the nasal crossed optic fibers causes bitemporal heteronymous hemianopsia, which may be peripheral, central or total, according to whether the site of the lesion is in the anterior, the posterior or the anteroposterior aspect of the optic chiasm. A lesion in the left or the right segment of the posterior pole of the optic chiasm or in the corresponding part of the optic tract causes right or left homonymous hemianopsia. If the lesion is located at a point on the optic tract before it reaches the anterior corpora quadrigemina, hemianopsia and motor disorders of the sphincter of the iris occur. If the lesion is located in the visual center of the calcarine fissure, or near this center, quadrantic homonymous hemianopsia, either superior or inferior, according to the site of the lesion, is produced. A lesion in an area of the cortex which is in communication with the cortical visual zone causes cortical or psychic blindness or else alexia. The Argyll Robertson pupil is a sign

of neurosyphilis. Adie's anisocoria is a neurotropic disorder. It is also a component of the Adie syndrome (encephalomeningopathy). Oculomotor paralysis on one side and hemiplegia on the opposite side (Weber's syndrome) indicates a lesion of the oculomotor nerve before it emerges from the lower border of the cerebral peduncle. Unilateral miosis, ptosis and enophthalmos (Horner's syndrome) result from paralysis of the cervical sympathetic fibers. Purely motor total ocular paralysis, of the Rochon-Duvigneau type, indicates a lesion of the oculomotor nerve in its course through the sphenoid fissure. Sensorimotor paralysis occurs when the ophthalmic nerve is also involved. Total motor-sensory paralysis occurs when the traumatic lesion or the tumor involves the optic tract. The sixth nerve is paralyzed in the Gradenigo syndrome, as a result of a lesion of the petrous bone, and also in association with other nerves in diseases of the pons which produce the Millar-Gubler syndrome (alternating abducens-facial hemiplegia). Corneal anesthesia (Oppenheim's sign) is an early sign of tumor of the cerebellopontile angle. The oculocardiac reflex shows the relations between the trigeminal and the spinal nerves. The various modalities of nystagmus during stimulation of the vestibular nerve are of value in the differential diagnosis of cerebellar and labyrinthine lesions, as well as in the diagnosis of the site of certain cerebral tumors.

W ZENTMAYER

#### POST-TRAUMATIC AND HISTAMINE HEADACHE A FRIEDMAN and C BRENNER, Arch Neurol & Psychiat 52:126 (Aug) 1944

Twenty-two patients with a history of headache following injury to the head received 0.1 mg of histamine base (0.275 mg of histamine diphosphate) intravenously.

Headaches were produced by this injection which in 13 patients were identical with the post-traumatic headaches in character and location and in 3 patients were strikingly similar. In 2 patients headache failed to develop.

The prompt decrease in systolic blood pressure after the injection of histamine was followed by a secondary rise which was nearly as great (22 and 18 mm of mercury, respectively). This rise was probably due to a response of the sympathetic nervous system produced reflexly by the primary changes incident to the injection of histamine.

Headache appeared as the blood pressure was rising.

The majority of the patients with histamine headache obtained some (occasionally striking) relief by sitting upright. This is inconsistent with reports in the literature that lowering of the intracranial pressure of the cerebrospinal fluid aggravates histamine headache.

It is possible that the injection of histamine activates the physiologic mechanism which is involved in the production of some types of post-traumatic headache.

The possibility that the injection of histamine may influence favorably the symptom of post-traumatic headache is suggested by results in some of our patients.

R IRVINE

#### Orbit, Eyeball and Accessory Sinuses

##### UNILATERAL PULSATING EXOPHTHALMOS CAUSED BY RUPTURE OF THE CAROTID ARTERY IN THE CAVERNOUS SINUS OF THE OPPOSITE SIDE. REPORT OF A CASE. F GEIS, Klin Monatsbl f Augenh 106:209 (Oct) 1941

A youth aged 18 fired a 6 mm caliber bullet into his right temple. He was able to return to work after about ten weeks, free from any disturbances except for a bruit, which increased while he was working or stooping. A week after he had resumed his work, or eleven weeks after the accident, he noticed that his left eye protruded. The bullet had passed through the right temporal bone behind the orbit and rested on the right side of the dorsum sellae at the right cavernous sinus. The presence of several bone splinters was noted in the roentgenogram. The oculomotor, trochlear and optic nerves were injured, while the abducens and maxillary nerves, located in the lower portion of the sinus, were intact. Rupture of the right internal carotid artery in the right cavernous sinus occurred and was followed by dilatation of the venous system, which caused pulsating exophthalmos on the opposite side, while the orbit on the side of the ruptured carotid artery remained unaltered. This type of crossed pulsating exophthalmos may occur if the blood stream returning from the cavernous sinus in the ophthalmic vein of the same side is blocked by tear, thrombosis or compression of the superior ophthalmic vein through splinters of bone or a foreign body. Previous enlargement of the intercavernous sinuses may further the development of crossed pulsating exophthalmos. The bruit ceased on compression of the carotid artery on the right (opposite) side and, later, after its ligation. It is advisable prior to ligation to find out by compression which carotid artery is the cause of a pulsating exophthalmos.

K L STOLL

#### Retina and Optic Nerve

##### EXUDATIVE RETINITIS (COAT'S DISEASE) C S DAMEL and A D GRAMMATICO, Arch de ofal de Buenos Aires 19:51 (Feb) 1944

A girl 18 years of age had involvement of both eyes. She was suffering from syphilis, probably hereditary. The general examination revealed nothing else of importance. The authors

had the opportunity to observe the patient for seven months and noticed that the exudate in the left eye, which was the last involved, changed from gray to white, this, according to them, furnished proof of the hypothesis that the condition has its origin in a degenerative process of the pigmentary epithelium

A full discussion of the etiopathology and differential diagnosis is given

H F CARRASQUILLO

TOXICITY OF ARSENICAL COMPOUNDS FOR THE OPTIC NERVE CONTRAINDICATIONS D LIVRAMENTO PRADO, *Arq brasil de oftal* 7 61 (April) 1944

According to Prado, the majority of persons with neurosyphilis have lesions of the optic nerve, latent, active or healed Syphilis gives to the nerve a special sensitivity to arsenicals, which is the cause of the development of optic neuritis in the course of arsenical therapy when the latter is given without primary treatment with bismuth or mercury The author advises a thorough ophthalmologic examination of the patients before administration of antisyphilitic treatment Any lesion of the fundus of the eye, even if healed, as well as keratitis or progressive diminution of the visual field, contraindicates immediate administration of arsenicals These patients should have bismuth or mercury therapy until the ocular lesion shows great improvement After a period of rest from the use of bismuth or mercury, arsenical therapy may be administered without danger of the development of optic neuritis

W ZENTMAYER

### Therapeutics

OCULAR THERAPY WITH PENICILLIN USED TOPICALLY, INTRAOCULARLY, AND SYSTEMICALLY C A MIETUS, *Am J Ophth* 28: 173 (Feb) 1945

Mietus gives the following summary

"1 Penicillin is a wonderful new therapeutic agent which can safely be added to the armamentarium of ophthalmologists

"2 Penicillin can be utilized in the three ways demonstrated in the foregoing case reports

"3 The use of penicillin by injection into the anterior chamber offers promise of beneficial results, and this mode of therapy warrants further investigation"

W S REESE

PENICILLIN IN OPHTHALMOLOGY J E L KEYES, *J A M A* 126:610 (Nov 4) 1944

Material for this report was derived from the special penicillin research center at Bushnell General Hospital, from private communications from medical officers of the Army and from medical literature on penicillin

Penicillin is the drug of choice in the treatment of ophthalmic diseases secondary to infection with gonococci, streptococci and sensitive staphylococci Penicillin should be given a trial in the treatment of diseases caused by *Neisseria meningitidis*, *Neisseria catarrhalis* and the pneumococcus The use of penicillin is optional in the treatment of infections caused by *Corynebacterium diphtheriae*, *Clostridium welchii*, *Actinomyces bovis* and *Treponema pallidum* In diseases due to noninfectious processes, such as allergy, the removal of a secondary infection by treatment with penicillin is helpful but obviously leaves the primary problem unsolved The use of penicillin as a prophylactic with certain intraocular operations and ocular injuries is recommended Early and large doses of penicillin are indicated in cases of orbital cellulitis secondary to infection in the paranasal sinuses and the adjacent dural sinuses

Solutions of penicillin, because of their instability, do not lend themselves to office and home medication as readily as do more stable drugs Penicillin ointment is reasonably stable for at least a month at room temperature and for six months in a commercial refrigerator Routes of administration and dosages are stated

The article, which is comprehensive, is illustrated

W ZENTMAYER

# Society Transactions

EDITED BY DR W L BENEDICT

## AMERICAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

CONRAD BERENS, M D, *Chairman*

ROBERT J MASTERS, M D, *Secretary*

*Ninety-Fourth Annual Session, Chicago  
June 12 to 16, 1944*

### The Making of an Ophthalmologist Chairman's Address DR CONRAD BERENS, New York

The medical curriculum of the ophthalmologist should include comprehensive courses in higher mathematics, biology, chemistry, physics and modern languages and, if possible, elementary courses in embryology, comparative anatomy, physiology, bacteriology and physiologic chemistry. In medical school the student should be permitted to elect certain subjects which will aid him in ophthalmology. After graduation from the medical school, a year of internship and two or more years of residency in an eye hospital or the ophthalmic department of a general hospital are most desirable. If possible, the student should have a course in the basic sciences related to ophthalmology before he enters active hospital work. One of the most important problems in ethics from the standpoint of public service and public health is that of optometry. The lack of cooperation between ophthalmologists and all others concerned with vision and health of the eyes is the most serious unsolved problem in the prevention of blindness today.

Participation in the scientific program at medical meetings is urged, so that the ophthalmologist will maintain his interest in general medicine, surgery and neurology.

### Diagnosis of Orbital Tumors Address of the Guest of Honor DR WILLIAM L BENEDICT, Rochester, Minn

The three cardinal signs of orbital tumor are, in order of their importance, exophthalmos, visual disturbances and changes in bone as revealed in roentgenograms. Exophthalmos is the most common of all these signs of tumor of the orbit. As it occurs also in all cases of space-taking or expansive disorders within the orbit, anterior or ocular displacement in itself is not indicative of the cause. Generally speaking, the rate of increase in proptosis is an index of the rate of growth or expansion of the space-taking lesion behind the eyeball, but when prop-

tosis is caused by a tumor, its extent is not truly indicative of the size of the lesion, as tumors of the anterior part of the orbit, particularly in the superior quadrant, will as a rule produce exophthalmos in the early stages of their development, and, since the globe occupies most of the space in the anterior third of the orbit, any extraocular growth displaces the eyeball as long as the bony wall stands firm. Tumor of the posterior half of the orbit, on the other hand, may acquire considerable size before appreciable proptosis occurs.

As most tumors of the orbit are unilateral, unilateral exophthalmos may be presumed to be due to a tumor unless there is some other evidence of cause for it. Bilateral exophthalmos due to tumors of the orbit is rare but is commonly present with Mikulicz' disease (achrocytosis of lacrimal gland) and with dysthyroidism. Angioneurotic edema and lymphoblastoma are also most frequently bilateral and may resemble neoplasms. Mucocoele, pyocoele or aneurysm causing exophthalmos is often undiagnosed or is mistaken for a tumor. To rule out goiter as a cause of exophthalmos may require observation of the patient under treatment for several months. Mikulicz's disease may closely resemble the orbital changes of hyperthyroidism.

Loss of visual acuity, with preservation of vision in the peripheral field, strongly indicates a postorbital or chiasmal lesion. When central loss of vision occurs before exophthalmos appears, the chances are greatly in favor of the lesion being due to an inflammatory process and of loss of vision being produced by such condition as retrobulbar neuritis.

In the absence of ophthalmoscopic changes, such as choked disk, optic neuritis, optic nerve atrophy, retinal and choroidal disease and opacities of the media, visual loss may be presumed to be due to changes along the visual pathways. The lesion may be retrobulbar and may be situated within the orbit. There is always the probability that it may be due to a tumor. Roentgenograms are useful in the identification of some orbital tumors. Osteomas of the sinuses that encroach on the orbit are best identified by this means. Hyperostosis of the orbital wall is brought about by tumors and diseases of the bone or of soft tissue that is situated near the bone.

Some vascular tumors that develop slowly along the orbital wall produce hyperostosis. Erosion of the walls is the rule in cases of pulsating tumor, although thickening of the lateral wall of the orbit may occur, as in cases of

hemangioma and pulsating exophthalmos. Exploration of the orbit for diagnosis should always be made through an incision large enough and so placed that, should a tumor be encountered or any other pathologic condition be found that would require surgical removal, the operation can be completed at the time. If one is not sure of the presence of a tumor, it is safe in most instances to apply roentgen therapy and await developments.

**Treatment of Bilateral Retinoblastoma (Retinal Glioma) Surgically and by Irradiation: Report on Progress** DR HAYES MARTIN AND DR ALGERNON B REESE, New York

This article was published in full in the June 1945 issue of the ARCHIVES, page 429

**Keratitis Neuroparalytica. Corneal Lesions Following Operations for Trigeminal Neuralgia** DR C L PANNABECKER, Ann Arbor, Mich

This article was published in full in the December 1944 issue of the ARCHIVES, page 456

#### ABSTRACT OF DISCUSSION

DR A D RUEDEMANN, Cleveland. In the treatment of trigeminal neuralgia the surgeon should not cut the first division of the nerve. After operation for trigeminal neuralgia the patient should be under the observation of a physician at home. His general health must be maintained.

MAJOR J M MASTERS, Medical Corps, Army of the United States. Impressions gained from the study of about 15 patients who were treated either by total or by subtotal posterior ganglionectomy or rhizotomy in the neurosurgical service of Dr E Vernon Hahn, of Indianapolis, were subsequently confirmed by the study of other patients similarly treated. Loss of luster of the corneal epithelium soon after operation, with the appearance of a faint gray path, was nearly always observed, causing apprehension of a catastrophe which did not always occur. From one to three days after operation a fine stippling of the involved cornea may be observed after staining with fluorescein. This stippling is seen much earlier than the more serious corneal complications mentioned by Dr Pannabecker. Their presence indicates cellular edema and fine exfoliation of the epithelium. Usually they leave five to seven days after operation without secondary scarring, but they have been observed to last many weeks without going on to ulceration. Frequent relapses may occur during the process of healing.

The observation has never been made in cases of subtotal rhizotomy in which the ophthalmic division of the nerve has been spared.

**Meridional Aniseikonia at Oblique Axes** DR HERMAN M BURIAN and DR KENNETH N OGLE, Hanover, N H

This article was published in full in the April issue of the ARCHIVES, page 293

#### ABSTRACT OF DISCUSSION

DR LAWRENCE T POST, St Louis. My studies on aniseikonia made personally on more than 450 patients, as well as less personal observations on about 700 patients during the past ten years, have been concerned with practice rather than theory. The figures which my associates and I have obtained indicate that about 80 per cent of patients for whom aniseikonic glasses were ordered were definitely helped and that almost 50 per cent were made entirely comfortable. Replies were solicited only from persons who had worn their aniseikonic correction for at least nine months.

The first question which arises is whether the major factor in this increased comfort is the correction of aniseikonia or something else, such as a change in the refractive correction made at the time the eikonic lenses were given or the psychologic effect of the elaborate examination. It may also be asked whether the patient could have been relieved by some procedure other than the giving of the eikonic glasses, for example, orthoptic training. I have the impression that the eikonic correction is by far the most important factor in producing this increased comfort.

Aniseikonia can never be fully evaluated clinically or the eyes attain their maximum usefulness until two conditions have been fulfilled. First, the test must be made available to every ophthalmologist, and, second, the cost of eikonic lenses must not be prohibitive to the average patient.

DR ERNEST A W SHEPPARD, Washington, D C. Early students of modern refraction and of ocular motility recognized deviations of the vertical meridians of the eyes. Stevens designated such a deviation as the declination error, and he and Savage emphasized its importance as a cause of asthenopia. The types of declination errors were not clearly understood, and therefore the treatment was unsatisfactory. Burian and Ogle have described three types, on the basis of the etiologic factors: (1) declination errors produced by cylindric lenses at oblique axes, (2) deviation errors associated with cyclophoria, and (3) deviation errors associated with basic meridional aniseikonia.

For diagnostic purposes it is more important to know the type than the degree. The methods of measurement used by the authors constitute an important advance both in refraction and in ocular motility, and they are to be congratulated on having recognized the association of the two conditions. The results they have obtained are most gratifying.



## Gonioscopic Correlates of Responsiveness to Miotics. DR PETER C KRONFELD, Chicago

This article was published in full in the December 1944 issue of the ARCHIVES, page 447

### ABSTRACT OF DISCUSSION

DR H ISABELLE MCGARRY, Chicago In cases of glaucoma of the narrow angle type, Dr Kronfeld mentions the frequent presence of pronounced angle pedicament without peripheral anterior synechias. In many cases in which the angles in the two eyes appear exactly the same, one eye may show a notable increase in tension, requiring miotics or surgical treatment or both, and the other eye may not show hypertension unless provoked by mydriasis. In the clinic my associates and I consider the eye with the normal pressure, normal fields and normal disks as preglaucomatous, and prevent mydriasis with miotics.

I, also, have been unable to come to any definite conclusion regarding glaucoma of the wide angle type and glaucoma secondary to uveitis.

DR JOHN M MCLEAN, New York Gonioscopy, while of restricted usefulness to the pure clinician, is a valuable tool in the hands of the clinical investigator. It has already demonstrated the fallacies of the theories which explain chronic simple glaucoma on the basis of anterior peripheral synechias. It has also shown that synechias are the result, not the cause, of chronic congestive glaucoma.

Dr Kronfeld had demonstrated a correlation between miosis itself and reduction of tension in certain cases of glaucoma of the iris block type. This does not hold true in all cases of this type, nor does it hold for other forms of glaucoma. Moreover, all who practice routine gonioscopy in the study of glaucomatous eyes find many cases in which there are open angles and an elevated intraocular pressure which responds to use of the miotic drugs.

DR C W ASCHER, Cincinnati If gonioscopic examination does not supply correlates of responsiveness to miotics, a test of the efficiency of the exhaust system can be performed in cases in which, under favorable conditions, the outflowing aqueous humor may become biomicroscopically visible. This occurs in a vein arising from the corneal limbus or, still farther away, in a vein leaving a scleral emissarium. These vessels which contain aqueous humor, either clear or mixed with blood, have been called aqueous veins.

Compression of the recipient vessel of an aqueous vein produces either expulsion of blood from the blocked section of the vessel or expulsion of clear fluid from the particular aqueous vein. In glaucomatous eyes the latter effect is the rule, indicating weak elimination of aqueous

humor from this aqueous vein, and possibly from the whole exhaust system, probably due to a transient or, in other cases, to a permanent narrowing of the immediate outlets of the canal.

Miotics, as well as surgical intervention, can reestablish a more vigorous flow in favorable cases, and then expulsion of blood from the blocked section of the vessel may be seen during the compression test performed on the aqueous vein.

## Choice of Operation in Glaucoma. DR PAUL A CHANDLER, Boston

Operation is nearly always indicated in cases of primary acute glaucoma. Iridectomy will not be successful in cases in which the condition has been neglected. In these cases a filtering operation of some sort must be done if tension is to be permanently controlled. Probably an iridencleisis with sclerectomy is the most effective operation. In cases of chronic glaucoma the choice of operation depends mainly on the personal preference of the surgeon. There are some situations, however, which seem to respond better to certain types of operation. Iridectomy is very effective in younger persons, particularly when the tension of the glaucomatous eye is relatively low. After the age of 60 iridencleisis is probably preferable, since it seldom produces hypotony and offers little trauma to the eye. With congested eyes iridencleisis with sclerotomy is very satisfactory. In general, the iris inclusion operation is chosen whenever an eye must be operated on in the presence of a relatively high tension.

## Dibutoline Sulfate. A New Mydriatic and Cycloplegic Drug. DR KENNETH C SWAN and DR NORMAN G WHITE, Iowa City

This article was published in full in the January issue of the ARCHIVES, page 16.

## Management of Traumatic Hyphema DR RALPH O RYCHENER, Memphis, Tenn

Traumatic hyphema following contusion rather than laceration of the globe is frequently complicated by secondary hemorrhage from the iris, increased intraocular pressure, staining of the cornea with blood, atrophy of the iris and persistent secondary glaucoma, which may result in atrophy of the optic nerve and staphyloma of the cornea. Most of these complications may be avoided or the effect nullified by simple paracentesis of the cornea as soon as the intraocular pressure is elevated, the procedure is also indicated when the anterior chamber is completely filled with blood, even though the pressure may still be normal. Surgical intervention should be carried out without delay whenever the intraocular pressure is increased or no clear aqueous is visible in the anterior chamber. It is possible that the use of miotics rather than mydriatics



immediately after injury will result in fewer secondary hemorrhages and in less necessity for surgical measures

#### ABSTRACT OF DISCUSSION

DR F BRUCE FRALICK, Ann Arbor, Mich Partial filling of the anterior chamber is not an indication for paracentesis. These hemorrhages usually absorb in a few days and seldom cause any elevation in tension. Complete filling of the anterior chamber with blood is definitely an indication for paracentesis, whether the tension is elevated or not. One should not wait for elevation of tension before doing the paracentesis.

By judicious use of this procedure, the course of the absorption period has been shortened and the incidence of hemorrhagic staining of the cornea has been lowered. My associates and I employ atropine in eyes displaying traumatic hyphemia with the thought of combating the associated iridocyclitis. Dr Rychener has suggested that miotics be used in place of atropine at this stage. There are no comparable statistics to support this preference, but from a pharmacologic point of view the use of a miotic should be more acceptable.

I am of the opinion that even after the initial period of hyperemia has disappeared atropine would still be indicated if circumcorneal flush and ciliary tenderness should develop, indicating the appearance of iridocyclitis.

DR HUGO L BAIR, Rochester, Minn. I prefer to perform the paracentesis with a keratome, since it provides an opening large enough to permit withdrawal of most of the blood clot and to allow satisfactory irrigation of the anterior chamber with isotonic solution of sodium chloride. It is important to withdraw or wash out as much of the clot from the angle of the anterior chamber as is readily possible without causing trauma to the structures there.

DR WILLIAM B CLARK, New Orleans. A dietary regimen for the relief of intraocular hemorrhage was offered.

To the exclusion of all other foods and liquid, the patient is given every two hours a mixture of 2 ounces (60 cc) of white Karo corn syrup and 6 ounces (180 cc) of fruit juice, which may be grapefruit, orange or pineapple. Except for a sedative, which the patient may require, nothing else is administered for a period of more than six days. The author reported rapid clearing of the hyphemia.

DR PAUL A CHANDLER, Boston. I have been accustomed to distinguishing two types of hyphemia. In one, no portion of the iris is visible, and the blood is almost black. In the other, some portion of the iris is visible, and the blood is red. In the first type, in which the blood is black, the surface of the clot is homogeneous. In the second type one can see structure in the clot. In cases in which the anterior chamber is black

with blood and the pressure is elevated, I have been accustomed to wash the clot out of the anterior chamber.

In cases in which any portion of the iris is visible and the blood is red, I thoroughly agree with Dr Rychener that irrigation of the anterior chamber is entirely too radical a procedure. A simple paracentesis can be done if necessary, but in all cases before such a procedure the use of miotics rather than mydriatics is of great importance.

#### Nonmagnetic Intraocular Foreign Bodies DR HARVEY E THORPE, Pittsburgh

Chemically inert intraocular foreign bodies need not be disturbed unless they produce mechanical irritation. They sometimes cause glaucoma.

Differentiation of magnetic from nonmagnetic foreign bodies can be aided by the history of the injury, examination of the tools employed and use of the Berman locator, as well as by examination of fragments from the face or other exposed parts of the body in explosion cases. The use of the magnet for diagnosis is bad practice and should be deprecated.

The presence of multiple intraocular foreign bodies, when they exceed three, suggests conservative therapy for the time being. One must avoid mutilating a globe simply for the sake of removing a foreign body that may be inert. Retinal attachment must be properly and promptly treated. Prompt removal of intraocular foreign bodies is important. The author uses his ophthalmic endoscope for removal of foreign bodies situated deep in the vitreous.

This paper was published in full, with discussion, in the January 27 issue of *The Journal of the American Medical Association*, page 197.

#### ABSTRACT OF DISCUSSION

DR E B SPAETH, Philadelphia. The accurate roentgenographic localization of a magnetic foreign body is relatively unimportant as long as one knows (1) the size and the shape of the foreign body, (2) whether the foreign body is intraocular or extraocular and (3) whether it is anterior or posterior to the iris-ciliary body-lens diaphragm. The use of any and all means available for localization—radiopaque markers, scleral rings, contact glasses, iodized oil and injections of air, molded films and filtered roentgen rays—is necessary, though perhaps not in any one individual case.

MAJOR MEYER H RIWCHUN, Medical Corps, Army of the United States. In cases in which an intraocular foreign body has been embedded for some time, sulfadiazine therapy may be instituted twenty-four hours prior to operation. Two grams is given at once, followed by 1 Gm every four hours for two days and then every six hours for two more days, after which its use

may be discontinued unless infection is present. The pars planum approach of Voerhoeft and Fialick is an excellent method of removing magnetic intraocular foreign bodies. It can be used occasionally with nonmagnetic foreign bodies if they are located in this convenient zone, a fine forceps being utilized instead of the magnet. The advantages of this method are absence of hemorrhage, little likelihood of detached retina and practically no danger of sympathetic ophthalmia.

#### Dacryocystitis: The Transplantation Operation

DR HAROLD GIFFORD JR, Omaha

This article was published in full with discussion, in the December 1944 issue of the ARCHIVES, page 485.

#### Chronic Dacryocystitis: Treatment from the Rhinologist's Point of View

DR LAVERNE B SPAKE, Kansas City, Kan

This article was published in full, with discussion, in the December, 1944 issue of the ARCHIVES, page 488.

#### SYMPOSIUM ON USE OF PENICILLIN IN TREATMENT OF DISEASES OF THE EYE, EAR, NOSE AND THROAT

#### Diseases of the Eye

LIEUTENANT COLONEL JOHN E L KEYES, Medical Corps, Army of the United States

Penicillin is the drug of choice in the treatment of ophthalmic diseases secondary to infection with gonococci, streptococci and sensitive staphylococci. The drug should be given a trial in the treatment of diseases caused by *Neisseria meningitidis*, *Neisseria catarrhalis* and pneumococci. Its use is optional in the treatment of infections caused by *Corynebacterium diphtheriae*, *Clostridium welchii*, *Actinomyces bovis* and *Treponema pallidum*.

The relief afforded by penicillin therapy when it is effective is usually prompt, in some instances startling and usually better than that afforded by other modes of medication. Considerable penicillin can be saved by identification of the bacteria present in a disease before treatment is instituted. A primary sensitivity test is recommended in cases of chronic infection caused by staphylococci. An unfavorable early response to the therapy suggests a reappraisal of the case. A virulent, resistant organism may be present.

The use of the substance as a prophylactic with certain intraocular operations and ocular injuries is recommended. Experience suggests that it is better practice to give an overdose than to give an underdose of the drug. Early administration of penicillin in large doses is indicated in cases of orbital cellulitis secondary to infection in the paranasal sinuses and adjacent venous dural sinuses.

#### Diseases of the Ear

CAPTAIN CLIFFORD A SWANSON (MC), U S N, and LIEUTENANT DANIEL C BAKER JR (MC), U S N R

Penicillin was found to be of value in the treatment of acute and chronic otitis media, acute mastoiditis and acute labyrinthitis. The drug was employed with success frequently when other forms of therapy had failed. It was possible either to avoid operation for acute mastoiditis or to use the drug with satisfactory results after operation had been performed. When the drug is instilled in the mastoid cavity after operation, healing is prompt and the period of convalescence is shortened.

#### Diseases of the Nose and Throat

CAPTAIN F J PUTNEY, Medical Corps, Army of the United States

Penicillin was used both locally and systemically at Bushnell General Hospital in treatment of some of the more severe and life-endangering infections of the nose and throat. These included orbital complications of disease of the paranasal sinuses, osteomyelitis of the frontal and maxillary bones, epidural abscess, cerebral abscess and thrombosis of the cavernous sinus. Penicillin therapy brought about prompt improvement, and in some cases spectacular results. In general, the acute infections responded more quickly and satisfactorily than the chronic ones.

#### ABSTRACT OF DISCUSSION ON SYMPOSIUM ON PENICILLIN

MAJOR ELMER A VORISEK, Medical Corps, Army of the United States. My associates and I have used penicillin in a dilution of 500 units per cubic centimeter. In cases of gonococcal ophthalmia the solution was instilled locally, 4 drops every hour, with disappearance of the organisms in conjunctival smears and cultures after twenty-four hours and no recurrences. Intramuscular injections were not given until after the ophthalmic infection was considered cured, except in a case in which the genital gonorrhea was cured with intramuscular injections, this recovery being followed two days later by gonococcal conjunctivitis in the socket of an eye which had previously been enucleated.

Even though negative smears and cultures of conjunctival scrapings may be obtained within twenty-four hours, irrigation with the solution of penicillin should be continued, but at less frequent intervals, until the results of three consecutive daily examinations are reported as negative. We have also used penicillin to irrigate the lacrimal passages in cases of chronic suppurative dacryocystitis, 2 cc of the 500 unit solution being used daily.

Several patients with orbital cellulitis with proptosis have been seen in consultation with the otolaryngologist, but in each instance penicillin was used intramuscularly, and in 1 case the

abscess also was irrigated with the penicillin. Not only did the cellulitis respond rapidly, but the purulent nasal discharge from all the sinuses promptly cleared up within forty-eight to seventy-two hours.

MAJOR WALTER J. AAGESEN, Medical Corps, Army of the United States. In our practice my associates and I give 25,000 units of penicillin intramuscularly every three hours day and night for twelve to fourteen days. Especially is this true when the offending organism is the staphylococcus. In cases of chronic mastoiditis, and especially in cases of the acute form with complications, I feel that convalescence is definitely shortened by the use of penicillin. It will not eliminate pus when there is inadequate drainage, and surgical treatment is still of primary importance. We have found the drug effective in treatment of acute otitis media.

COMDR E. E. KOEBBE (MC), USNR. My associates and I have treated several hundred patients with early acute otitis media by means of penicillin, and the results have been universally good. We give 15,000 units every three hours around the clock for about seven days, or until the inflammation in the ear drum resolves and the landmarks return. Then we reduce the dose to 10,000 units and maintain that dosage three or four days, after which we give doses of 5,000 units for three or four days longer. We have treated 22 patients with meningitis complicating otitic infection in this way.

We have treated 15 patients with thrombosis of the lateral sinus. In all cases a positive blood culture or occlusion of the lateral sinus or both was demonstrated by operation. Penicillin alone is inadequate in treating thrombosis

of the lateral sinus. An operation is necessary, but in no case have we ligated the jugular vein.

CAPT ROBERT HENNER, Medical Corps, Army of the United States. A patient treated with sulfadiazine for about seventy-two hours became moribund and comatose and had a temperature of over 105 F. Institution of intravenous injections of penicillin combined with the intravenous use of a solution of heparin rapidly resulted in a negative blood culture for the Staph aureus that was previously present, and after a period of recovery of over six weeks he was returned to full duty.

CAPT F. J. PUTNEY, Medical Corps, Army of the United States. I should like to confirm the observation that in cases of thrombosis of the lateral sinus operation must be performed, in addition to treatment with penicillin. My associates and I have treated 8 patients with sinus thrombosis, and in each case the sinus was opened, in a goodly number, however, we were unable to remove the thrombus in the lower end of the sinus, at the jugular bulb, and, also, in these cases we did not ligate the jugular vein.

CAPT C. A. SWANSON (MC), USN. At the National Naval Medical Center, Bethesda, Md., the Penicillin Committee has now allowed penicillin to be used initially in cases of acute otitis media in place of the sulfonamide drugs. This therapy should give even better results. The days before penicillin came into use, it was the experience of my colleagues and myself that mastoid wounds took at least three weeks to heal. We have had only 3 cases in which penicillin was used locally in the mastoid wound, and in all 3 cases healing occurred in eight days.

## Book Reviews

Frederick II, Emperor of the Holy Roman Empire. *The Art of Falconry, Being the De arte venandi cum avibus*. Translated and edited by Casey A. Wood, M.D., and F. Marjorie Fyfe Price, \$10 Pp 637, with illustrations. Stanford University, Calif. Stanford University Press, London Oxford University Press, 1943

Dr Casey A. Wood, in searching the mysteries of the organ of vision, sought the solution of the capacity of sight in the eyes of birds. It is well known how patient were his ophthalmic studies of birds at the zoologic gardens and elsewhere, which he described and illustrated in "The Fundus Oculi of Birds, Especially as Viewed by the Ophthalmoscope. A Study in Comparative Anatomy and Physiology" (Chicago, Lakeside Press, 1917). Later, on a sojourn to British Guiana, he gathered heads from the flocks of the many varieties of birds migrated there from the colder countries, which should serve as specimens for later histologic study. His interest in avian subjects, however, led him to the realization that to comprehend them he, necessarily, should become more or less seriously an ornithologist. Yet, in that new study he always maintained that his primary object was to learn more and more about the mysteries of sight. Quite naturally, he eagerly sought most from the nature of birds of prey and rapacious birds, hoping to discover the source of the marvelous power which enables them to detect their quarry at long, long distances, remote from the point of their rising into the air. The habits of buzzards, eagles, hawks and other rapacious birds are well known to every one who has spent much time in the wilds. One is led to wonder. Is it sight or smell that incites one of a flock of buzzards sailing in circles high up in the air suddenly to dart down into the plain and seize a rabbit or squirrel which had moved out from the thicket?

(This reviewer recalls, while on the voyage from the ophthalmologic congress held at Amsterdam, the extraordinary flights of a pair of English sparrow hawks which had lived for several weeks on the ship, roosting in the shrouds stretched from the foremast. While apparently simply resting, though the seas were rough and black from the skies being overcast, they would suddenly dart over the ocean to alight at a far distant trough and then return as swiftly as they had left, carrying a small petrel struggling in their talons, which they proceeded to devour while clinging to the ropes. Thus they manifested, in the midst of conflicting lights and

shadows, visual acuteness beyond the human observer's acquiring.)

Through this aspect of his investigations, Dr Wood became deeply interested in the medieval practice of "Hawking," an interest which led him to delve into the life history of that prince of hawkers, King Frederick II, of Hohenstaufen (1194-1250). To that history Dr Wood devoted the last years of his life, with the highly efficient assistance of his niece, Miss Fyfe, preparing for publication a monumental and beautiful volume on "Falconry," in translation of Frederick's "De arte venandi cum avibus," from manuscripts prepared by the king up to the middle of the thirteenth century.

King Frederick should be of interest to the medical profession, as he did much to advance medical education and to regulate practice. By his edicts, there were required three years in premedical studies, a five year course of medical study, followed by a year of practical work, and, in order to receive the license, an examination by the state.

This work should be of interest to ophthalmologists, although it is not an ophthalmologic treatise, because it describes minutely the practice of hawking and the several varieties of hawks and because the whole success of that practice depends on the visual powers of another order of animal. A brief chapter on the eyes of the birds describes simply the gross appearance of the organ in the varieties employed.

The book is both a contribution to the history of science and an account of a distinct element in medieval culture. In itself, the volume is surpassingly beautiful, containing 186 plates, which can serve as an iconography of falconry. And it stands as a monument to American scholarship and the art of the printing and making of books.

BURTON CHANCE

**Doctors at War.** Edited by Morris Fishbein, M.D., with 15 other contributors. Price, \$5 Pp 418, with 82 photographs, charts and diagrams. New York: E. P. Dutton & Co., Inc., 1945.

In World War I 81 per cent of the wounded died, in World War II it was only 33 per cent. In the former conflict the death rate from disease was 156 per thousand, in the latter, only 06. This book tells how the reduction was accomplished. The Surgeons General of the Army and Navy describe the work of their departments in general. Surgery is discussed by Brig Gen F. W. Rankin, air medicine, by Maj Gen D. N. W. Grant, and convalescence and rehabilitation,

by Col H A Rusk Maj Gen P R Hawley, describes medical preparation for D-Day, and Capt F R Moore recalls his medical activities on Guadalcanal and Tarawa. On the civilian side, Surgeon General Parran describes the Public Health Service in wartime, Dr C W Griffiths writes of the Veterans Administration, Dr G Canby Robinson discusses the American Red Cross, Dr G B Darling, the National Research Council, and Dr H S Diehl, the doctor's work at home. Allocation of medical services is taken up by Maj Gen George F Lull, and selective service is discussed by Col L G Rowntree.

The magnitude of the medical tasks undertaken by the armed forces can hardly be grasped by a layman. He will be impressed by figures and statistics, but he will only sense the sacrifices of life, health and prospects implied in every line of this text.

The medical officer may well be proud of himself and his record, but he should enjoy his feeling of self respect while he can. The poor devil has worries enough, but it may be salutary for him to read a significant interpretation of his effort and sacrifice.

"It is interesting to note," writes a reviewer of this book in the *New York Herald Tribune* of May 13, 1945, "how much can be done by doctors where there are no private patients, no fees, and no patient has the right to choose his doctor." The politicians are already preparing

the welcome and the reward for the "doctor at war."

COMDR G M BRUCE

**Neuro-Ophthalmology** By Donald J Lyle, B S, M D, F A C S Price \$10.50 Pp 398, with 7 charts and 529 illustrations, Springfield, Ill Charles C Thomas, Publisher, 1945

Dr Lyle has presented a seemingly complex subject in such an interesting way that all ophthalmologists should be stimulated to start and/or continue the application of neurology to ophthalmology, inasmuch as the two are inseparable.

This book is profusely illustrated with original charts, fundal photographs, roentgenograms and visual field charts to correlate the anatomic, neurologic and ophthalmologic changes produced by developmental, inflammatory, vascular, neoplastic and traumatic lesions affecting the central nervous system. The extensive bibliography is more than sufficient to stimulate collateral reading.

Although the common and rare ocular syndromes are described, the ophthalmologic position usually is quite overshadowed by a too detailed anatomic and neurologic description. But, all in all, Dr Lyle's book is a much needed addition to every library and is highly recommended. The author is to be congratulated for a job well done.

W I LILLIE

# Directory of Ophthalmologic Societies \*

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All correspondence should be addressed to the Secre-  
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Last Friday of each month

\* Secretaries of societies are requested to furnish the  
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## EFFECT OF LOCAL ANESTHETICS ON CELL DIVISION AND MIGRATION FOLLOWING THERMAL BURNS OF CORNEA

GEORGE K. SMELSER, PH.D., AND V. OZANICS, M.S.

NEW YORK

It has long been recognized that the frequent topical application of anesthetics delays the repair of epithelial injuries of the cornea. This observation has been made clinically (Stallard<sup>1</sup>), and more rigorously controlled comparisons have been made on laboratory animals on which treated and untreated standardized corneal abrasions have been inflicted (Gundersen and Liebman,<sup>2</sup> Friedenwald and Buschke<sup>3</sup>). Such studies have led to attempts to secure less harmful drugs which are yet effective anesthetics.

The search for an anesthetic agent which does not inhibit healing is obviously of practical value. It is of equal interest to determine whether inhibition of healing processes is proportional to the anesthetic properties and is, therefore, possibly due to the same factors which produce anesthesia. In such a case normal healing rate and anesthesia would be incompatible. It is the purpose of this paper to show that anesthesia and normal healing are compatible, to compare the effect of various anesthetics on cell division and migration of regenerating epithelium and to indicate some drugs which produce adequate surface anesthesia and yet inhibit healing very little.

There are two processes involved in the healing of epithelial wounds: (1) cell migration, to cover the injured area, and (2) mitosis, to reconstitute the normal number of epithelial cells. It has been generally accepted that the

migratory activity occurs first and the cell division second. In the repair of small wounds, mitosis was found actually to decrease during the migratory phase (Arey,<sup>4</sup> Wigglesworth,<sup>5</sup> Arey and Covode,<sup>6</sup> Mann,<sup>7</sup> Friedenwald and Buschke<sup>3</sup>).

In earlier experiments (Smelser and Ozanics<sup>8</sup>) considerable mitotic activity was noted during the migratory phase of healing following rather extensive thermal burns of the cornea. In these experiments the number of mitotic figures found in the burned eye was greater than that found in the intact, control, eye in 84 per cent of the animals studied. These results were based on a study of thermal burns covering about one third of the cornea, whereas the earlier experiments of Arey, Arey and Covode, and Friedenwald and Buschke were concerned with small abrasions. In other experiments it was shown that abrasions, similar in size to the burns, healed in 64 per cent of the cases without significant increase in the number of mitoses.

Since cell division appears to play a role early in the healing of thermal burns, and since this type of injury was readily reproducible and produced no obvious damage to the substantia propria, it was decided to investigate the effect of anesthetic drugs on the healing of thermal burns.

Male rats of the Sherman strain, 80 to 105 Gm. in body weight and 5 to 6 weeks of age, were used. Comparisons of the effect of various drugs were drawn between litter mates. The horizontal band-shaped burns were produced with a Shahan thermophore equipped with a terminal fitted to the curvature of the rat's cornea. The animals were operated on while under

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1. Stallard, H. B. Methods of Anesthesia and Analgesia for Ophthalmic Operations, in Ridley, F., and Sorsby, A. Modern Trends in Ophthalmology, London, Butterworth & Co., Ltd., 1940, chap. 49.

2. Gundersen, T., and Liebman, S. D. Effect of Local Anesthetics on Regeneration of Corneal Epithelium, *Arch. Ophth.* **31**:29 (Jan.) 1944.

3. Friedenwald, J. S., and Buschke, W. The Influence of Some Experimental Variables on the Epithelial Movements in the Healing of Corneal Wounds, *J. Cell & Comp. Physiol.* **23**:95, 1944.

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7. Mann, I. Study of Epithelial Regeneration in Living Eye, *Brit. J. Ophth.* **28**:26, 1944.

8. Smelser, G. K., and Ozanics, V. Effect of Chemotherapeutic Agents on Cell Division and Healing of Corneal Burns and Abrasions in the Rat, *Am. J. Ophth.* **27**:1063, 1944.

ether anesthesia, with the same technic as that described earlier.<sup>8</sup> The thermophore (71 C) was applied for five seconds to both eyes, and autopsy was performed twelve hours later. The material to be tested was placed on the right eye every two hours during this period, and the rat was held so that the solution or ointment remained on the cornea and conjunctiva for one minute. Thus the epithelium was in contact with the drug for a minimum of five minutes during the twelve hour period. After treatment the rats quickly rid themselves of the ointment or solution. The eyes were fixed in Bouin's fluid, and the outline of the burned area was drawn with a camera lucida at a magnification of 30 diameters. Untreated burns, of the size studied, became covered with epithelium in fourteen hours and were nearly healed in twelve hours. Camera lucida drawings were made of the treated and the control burns. The edge of the regenerating epithelium was clearly visible in the eyes fixed in Bouin's fluid. Since the wounds were nearly healed, the area drawn was almost in a plane, however, when the injured area was still large, the area represented in the drawing was a little less, owing to the projection of a curved surface on to a plane one. This resulted in a conservative estimate of delays in healing. The area of the unhealed portion of the burn was determined by planimetric measurements of the drawings. The eyes were then embedded and sectioned, and the number of mitotic figures in the regenerating epithelium was counted. Sufficient counts were made so that repeatable values were obtained. The technic and the statistical methods used were the same as those reported earlier. The effect of the treatment given was judged in each case by comparing the mitotic figure counts and the residual area of the burn of the treated and the control eye of the same animal. These burns were found to be reproducible. In a series of 10 rats both eyes were burned and no treatment was applied. Both eyes healed at essentially the same rate, and the number of mitotic figures found in the right and the left eye was not significantly different in any case. The average area of the burn in the right eye of these rats varied only 7 per cent from the average area of the burn in the left eye. Variation between individual rats, however, was much greater.

#### EFFECT OF ANESTHETICS ON CELL DIVISION IN THE INTACT EPITHELIUM

As a preliminary to the experiments on regenerating epithelium, the effect of several anesthetics on mitosis in the intact corneal epithelium was determined. No apparent damage of the cornea was produced by these experiments, such as was described by Baba,<sup>9</sup> who used the drugs in much greater concentrations. Solutions of cocaine hydrochloride, 0.5 per cent, tetracaine (pontocaine) hydrochloride, 1 and 0.5 per cent, nupercaine hydrochloride, 0.5 per cent, phenacaine (holocaine) hydrochloride, 2 and 0.5 per cent, butacaine sulfate, 2 per cent, and chlorobutanol, 1 per cent, and ointments containing butyl aminobenzoate (butesin), 0.75 per cent, orthoform, 2 per cent, and butacaine (butyn) sul-

fate, 2 per cent, and metapen 1 3,000 were used.<sup>9a</sup> The aqueous solutions were unbuffered and contained 1 per cent sodium chloride, except the preparation of butacaine sulfate, which was made up in distilled water. The pH of the solutions, determined with a glass electrode, ranged from 4.0 to 6.0. These preparations were placed on one eye for one minute each hour for eight hours. The eyes were fixed and sectioned, and the number of mitotic figures in the epithelium was counted in each eye. The ratio of the number found in the treated to that in the untreated, control, eye was expressed as a per cent and the significance of the difference calculated.

The results of these experiments are shown in a bar graph (fig. 1). Application of all but four of these compounds inhibited cell division, when concentrations which are useful clinically were employed. Whereas the average depression of mitosis caused by 0.5 per cent cocaine hydrochloride and 1 per cent tetracaine hydrochloride

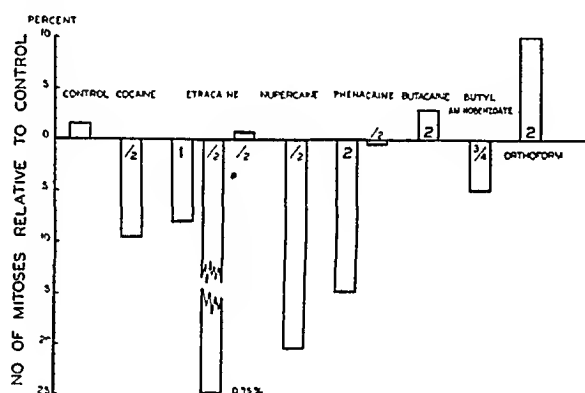


Fig. 1—Effect of anesthetics on mitosis in the intact corneal epithelium. Each bar represents the average of 4 to 7 eyes, the control, the average for 10 eyes. The figures in the bars represent the concentration of the drug expressed as a per cent.

was slight, both 0.5 per cent nupercaine hydrochloride and 2 per cent phenacaine hydrochloride caused a rather marked decrease in the number of mitotic figures found in the treated corneas. More dilute solutions of tetracaine and phenacaine had no deleterious effect on cell divi-

9a The solutions of cocaine hydrochloride were obtained in the hospital pharmacy. The solutions of all other drugs were prepared in our laboratory. Some of the ointments were also prepared in our laboratory in the hydrous wool fat base mentioned, others were proprietary ointments, obtained as follows.

Ophthalmic Ointment Butyn Sulfate 2% and Metapen 1 3,000, Abbott Laboratories, Ophthalmic Ointment Butesin Picrate 1% and Butesin 1%, Abbott Laboratories, Pontocaine Base Eye Ointment (0.5 per cent tetracaine base), Winthrop Chemical Company, Inc., Nupercainol (nupercaine base, 1 per cent), Ciba Pharmaceutical Products, Inc., and Holocaine Hydrochloride (2 per cent phenacaine hydrochloride), Abbott Laboratories. These products were purchased locally.

9 Baba, H. Vergleichende Beobachtungen über die durch Instillationen von verschiedenen lokalen Anaesthetica hervorgerufenen Augenveränderungen, abstracted, Zentralbl f d ges Ophth 40 555, 1938.

sion in the cornea Butacaine sulfate 2 per cent, was the only drug tested which could be applied in so great a concentration without causing a decrease in the number of mitotic figures Applications of an ointment containing 2 per cent butacaine sulfate likewise did not affect cell division. Two fat-soluble anesthetics were studied, butyl aminobenzoate and orthoform These compounds were dissolved in a hydrous wool fat base (anhydrous wool fat, 75 per cent, water 25 per cent) in concentrations of 0.75 and 2 per cent, respectively Neither preparation markedly affected cell division The data obtained for the orthoform group were somewhat variable, in 2 of the 5 tests definitely more mitoses were found in the treated cornea, thus raising the average response in this group The 6 animals treated with chlorobutanol also gave a somewhat surprising and variable response Four of the 6 corneas treated with chlorobutanol had more mitotic figures in the epithelium than the untreated, control, cornea One animal showed a definite depression

These experiments show that most of the anesthetics tested affected mitosis adversely This effect is, of course, modified by the concentration of the drug used, the route of administration and the frequency of application This last factor was tested with tetracaine Instead of the application of 0.5 per cent solutions once an hour, which was shown to have no effect on cell division, three applications an hour were made The technic was not otherwise varied The frequent, in contrast to the hourly, application of tetracaine was found to cause an extreme and consistent depression in cell division (75 per cent fewer figures than in the control eye)

The effect of subconjunctival injections of anesthetics on corneal mitosis was studied with cocaine hydrochloride, 1 per cent, and procaine hydrochloride, 2 per cent, in 8 animals This type of experiment was difficult to evaluate because the volume of solution injected (0.05 cc) was so great relative to the volume of the globe and orbit that some displacement of the soft tissues was probably produced The results, therefore, are not comparable to those of subconjunctival injections in man The corneas were fixed for study five to seven hours after the injections At this time there was a marked depression in the mitotic figures seen in the eye in which cocaine had been injected The effect of procaine, as would be expected, was less pronounced, though consistent, the number of figures found averaged 20 per cent less than in the control eye When 2 per cent procaine hydrochloride was made up in a solution of epi-

nephrine hydrochloride (1:2,500) no mitotic figures at all were found in the corneal epithelium of the eye in which the anesthetic was injected This result may have been due in part to a prolongation of the effect of procaine, but undoubtedly the epinephrine itself inhibited cell division (Friedenwald and Buschke<sup>10</sup>)

#### EFFECT OF LOCAL ANESTHETICS ON MITOSIS IN REGENERATING EPITHELIUM

In general, anesthetics had a more pronounced depressing action on mitosis following burns than in the intact epithelium (fig. 2), even though the drugs were applied once in two hours instead of every hour, and in some cases in lower concentrations Two exceptions to this rule, phenacaine and butyl aminobenzoate, were noted Both of these drugs interfered less with cell division in regenerating than in normal epithelium When the more dilute preparations, 0.5 and 0.75 per

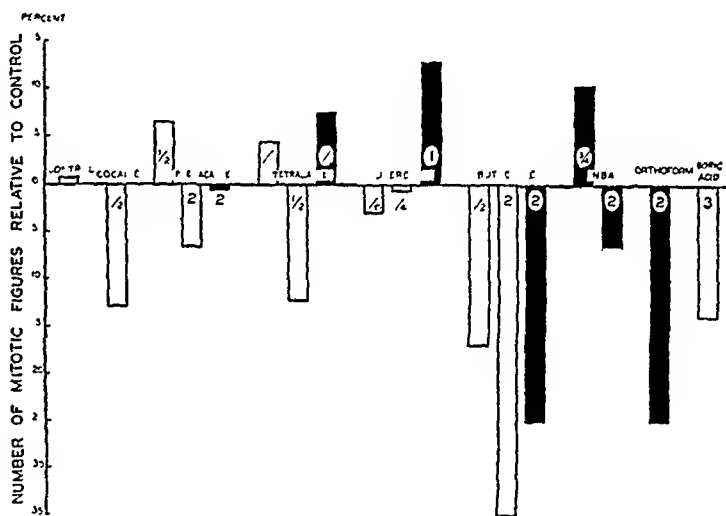


Fig. 2—Effect of anesthetics on mitosis in the corneal epithelium twelve hours following a thermal burn. Each bar represents the average for 5 to 7 eyes. The right eye of each animal was treated with the anesthetic, the control is the other, untreated but burned, eye of the same animal. The figures in the bars represent the concentration of the drug expressed as a per cent. N. B. A. indicates normal butylaminobenzoate.

In this figure the hollow bars represent aqueous solutions, the black bars, ointments.

cent, were applied, more mitoses were seen than in the untreated control burns of the other eye, however, the increase could not be considered statistically significant in either case.

The anesthetics may be arranged in order of their inhibitory action on cell division in the regenerating epithelium. Butacaine sulfate was the worst in this respect (fig. 2). Since aqueous solutions of butacaine sulfate also retarded

<sup>10</sup> Friedenwald, J. S., and Buschke, W. The Effects of Excitement, of Epinephrine and of Sympathectomy on the Mitotic Activity of the Corneal Epithelium in Rats, *Am J Physiol* 141: 689, 1944.

epithelization, the resulting smaller epithelial area may of itself have led to somewhat lower counts. Cocaine and tetracaine, which were next, and essentially equal, inhibited mitosis less. Phenacaine, butyl aminobenzoate and nupercaine were the best in that their application did not greatly affect the number of mitotic figures present in the healing burn. It is notable that the effect of butacaine and orthoform was very different on the injured and on the intact epithelium. The difference in the effect of nupercaine on the intact and the burned epithelium was probably due to the lower concentration used.

The superiority of ointments over aqueous solutions of several drugs was particularly noticeable in their effect on mitosis. Ointments containing 2 per cent butacaine sulfate (two preparations) inhibited cell division less than 2 per cent aqueous solution applied with the same frequency. Phenacaine, tetracaine and nupercaine ointments had no deleterious effect on

with those of Friedenwald and Buschke<sup>11</sup> on the effect of some anesthetics on cell movement in vitro. All of the compounds studied slowed this process but differed in the degree of the effect produced (fig 3). It appeared that migration was more easily inhibited than mitosis, although an exception to this rule (butacaine ointment) was found. The effect of each drug was highly consistent, since an inhibition was always produced, although it was variable in its severity. Just as the drugs studied could be rated in their effect on mitosis, a similar tabulation was possible with respect to their influence on cell migration. Aqueous solutions of nupercaine had, of all of the drugs tested, the greatest inhibitory action on cell movement. A 0.1 per cent solution of nupercaine hydrochloride was approximately equal to a 0.5 per cent solution of cocaine hydrochloride in this respect. In the table, the drugs are listed in descending order of their adverse effect on this healing process. Factors other than the active drug itself, such as the  $p_H$  or the tonicity of the solutions, may have been responsible for some of the inhibitory action. A solution of boric acid,  $p_H$  4.1, inhibited cell migration, but to a slight extent as compared with the anesthetics.

The two fat-soluble drugs, orthoform and butyl aminobenzoate, were dissolved in hydrous wool fat and applied as ointments. In 2 per cent concentration they both inhibited cell migration rather markedly, though less than the other drugs in aqueous solutions of similar concentrations (fig 3). Control tests with the same hydrous wool fat base also hindered cell migration but no more than did a solution of boric acid. A mixture of 1 per cent butyl aminobenzoate and 1 per cent butesin picrate made up in petrolatum was much less detrimental to cell migration than the butyl aminobenzoate alone in hydrous wool fat.

In addition to the experiments with solutions, four of the drugs, nupercaine, butacaine, tetracaine and phenacaine, were also applied as ointments. A comparison of the results of the application of anesthetics in these two forms on cell migration is shown in figure 4. The ointment base varied in the four preparations, and two of the drugs (nupercaine and tetracaine) were in the form of their bases, whereas phenacaine and butacaine were salts. In all four series the ointments had a far less deleterious effect than did the solutions. Ointments of nupercaine base, butacaine sulfate and phenacaine hydrochloride

11 Friedenwald, J. S., and Buschke, W. Mitotic and Wound-Healing Activities of Corneal Epithelium, *Arch Ophth* 32:410 (Nov.) 1944.

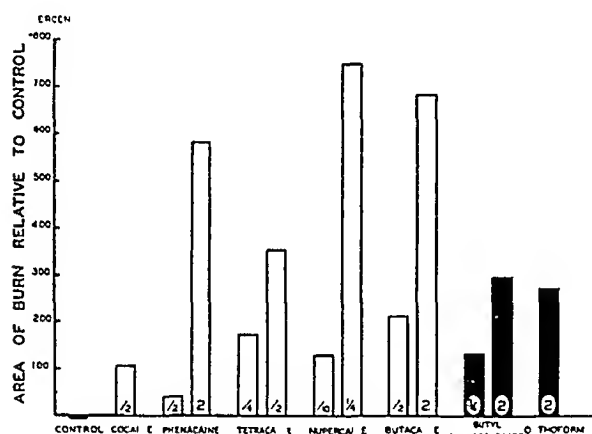


Fig 3—Influence of anesthetics on the healing of corneal burns. Each bar represents the average area of treated corneal burns relative to the average area of the untreated burns in the opposite corneas of the same animals. The measurements were made twelve hours after injury with a planimeter from camera lucida drawings. Five to 10 animals are represented by each bar. The hollow bars represent aqueous solutions, the black bars, ointments.

mitosis, whereas aqueous solutions of these drugs reduced the number of mitotic figures found. The nupercaine and tetracaine ointments contained the drug as its base rather than as the salt, which was used in the other cases.

#### EFFECT OF LOCAL ANESTHETICS ON CELL MIGRATION IN A REGENERATING EPITHELIUM

The second phase of healing, i. e., migration of the epithelial cells to cover the denuded stroma, was also notably inhibited by some of the anesthetics. This observation is in agreement

did not inhibit healing more than a hydrous wool fat ointment, whereas the aqueous solutions of these compounds greatly retarded this process. Indeed, the injuries treated with solutions of nupercaine hydrochloride and butacaine sulfate had remained at nearly their initial size for twelve hours, while untreated control burns had almost completed epithelization. Such an enormous difference between the solutions and the ointment was not found with tetracaine, however, this drug was used in lower concentration (0.5

in concentration, the superiority of the ointment over the solution is obvious. A 1 per cent solution of nupercaine hydrochloride is too great a concentration to use on the injured eye.

It is obvious from the foregoing observations that the drugs tested differed in their effect on the two processes studied. In general, the ointments were preferable to the solutions, and of these, phenacaine and nupercaine ointments had the least effect on either process. If mitosis is disregarded, butacaine ointment ranks with these

*Relative Effect of Anesthetics on Mitosis in the Intact, and Cell Division and Migration in the Burned, Corneal Epithelium*

	Most Inhibitory	Aqueous Solutions	Least Inhibitory
Intact Mitosis	Nupercaine,	cocaine, phenacaine = tetracaine,	butacaine
Burned Mitosis	Butacaine,	cocaine = tetracaine, nupercaine, 0.25%,	phenacaine
Migration	Nupercaine,	tetracaine, butacaine, cocaine	phenacaine
		Ointments	
Intact Mitosis	Cocaine, 0.5%,	butyl aminobenzoate, 0.75%, butacaine sulfate, 2%,	orthoform, 2%
Burned Mitosis	Orthoform, 2% = butacaine sulfate, 2%,	butyl aminobenzoate, 2%,	phenacaine hydrochloride, 2% = tetracaine base, 0.5% = nupercaine base, 1%
Migration	Orthoform, 2% = butyl aminobenzoate, 2%,	tetracaine base, 0.5%, nupercaine base, 1%,	phenacaine hydrochloride, 2% = butacaine sulfate, 2%

\* The order in which the drugs are listed should not be considered as an indication of their absolute position in the series, for many were approximately equal in their effect (indicated by =). The comparisons were made between equal per cent concentrations except where noted.

per cent) than were most of the others. It will be noted that an ointment containing 1 per cent nupercaine base was compared with 0.25 per cent solution of the salt. Even with this difference

in the slight effect on migration, tetracaine ointment, on the other hand, did not interfere with mitosis but delayed cell migration more than did the others.<sup>11a</sup>

#### COMMENT

The experiments just described confirm the well established opinion that many anesthetics interfere with healing. They show, further, that the drugs commonly used vary in their effect on healing, as they also do in their ability to pro-

11a Since this article was submitted for publication, we have carried out similar experiments with metycaine hydrochloride (Lilly) solutions and ointments. The burned areas, treated with a 1 per cent solution of metycaine hydrochloride, were 134 per cent larger than the untreated control burns. This delay in healing was similar to that caused by a 0.1 per cent solution of nupercaine hydrochloride. There were 17 per cent fewer mitotic figures in these treated eyes, a depression similar to that caused by butacaine sulfate. The ointment containing 4 per cent metycaine hydrochloride delayed epithelization a little less than did the ointment containing 0.5 per cent tetracaine base. The burned area was 159 per cent greater than the average area of the control burns. The number of mitotic figures was 25 per cent less in the ointment-treated eyes, an effect similar to that obtained with the ointment containing butacaine sulfate, 2 per cent, and metaphen

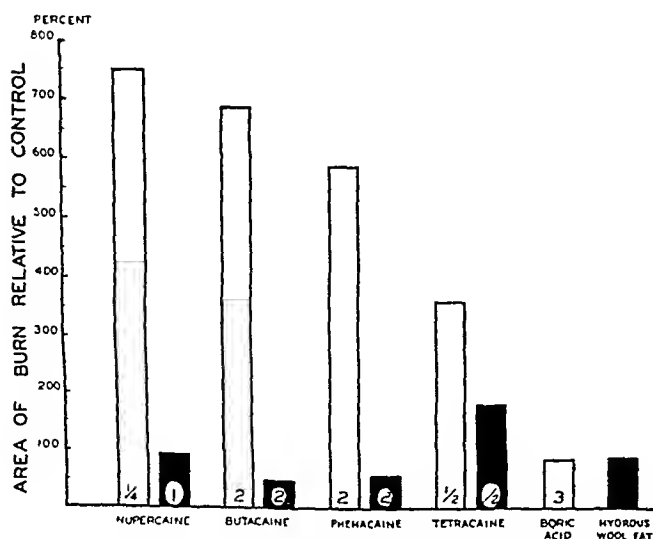


Fig 4—Comparison of the inhibitory effect of anesthetic ointments and solutions on epithelization of corneal burns. Five experiments are represented by each bar. (Some of the data are the same as those shown in figure 3.) All of the data were obtained as described in the legend of figure 3. The hollow bars represent aqueous solutions, the black bars, ointments.



duce anesthesia. It has been possible to classify the several drugs approximately in the order of their inhibitory effect on these processes (table). In addition, it appears that an anesthetic does not necessarily affect mitosis and cell migration equally.

Although cell division and cell migration both involve the movement or flowing of protoplasm and the biologic basis for both processes may be fundamentally the same, the two processes can be inhibited separately, and cell migration appears to be much more easily inhibited by some drugs than cell division. For example, aqueous solutions of phenacaine and nupercaine markedly inhibited cell migration but had no appreciable effect on the number of mitotic figures found in the epithelium of these corneas. The reverse condition was found to obtain when a butacaine and metaphen ointment was employed. An explanation of the basic mechanism involved would undoubtedly take account of the action of the drugs on the intracellular physiology of these processes, as shown in the studies of Michaelis and Quastel,<sup>12</sup> and of Herrmann, Moses and Friedenwald<sup>13</sup> on narcotics and respiratory enzymes. A second possibility which should not be ignored is suggested by the fact that some of the drugs used (nupercaine) were rather good detergents. It may be that this property is responsible in part for the inhibition of epithelization. Strong detergents would act in this manner, furthermore, when the drugs were incorporated in ointments, in which the detergent action would be reduced, they failed to delay significantly cell migration.

Although for the purposes of the experiment the drugs were applied frequently, once every two hours, it is worth while to note that the complete anesthetization of the cornea with several applications of cocaine produced an effect which was readily discernible under the conditions of our experiments many hours later, presumably long after the anesthesia had worn off. Comparison of the effects of various anesthetics, made on the basis of the molar rather than the per cent concentration of the drugs, would provide a more exact basis on which to rate the different compounds. However, the drugs used, except butyl aminobenzoate and orthoform, were fairly similar in molecular weight, 1 per cent solutions varying from one-thirty-fifth to one-thirty-ninth molar. Therefore,

in view of the nature of the experiments, satisfactory comparisons may be made on a percentage concentration basis.

The fact that more mitotic figures were found in the eyes treated with some of the drugs (fig 2) was not interpreted as due to stimulation of mitosis. The data were variable and the differences not statistically significant.

A more interesting and practical basis for comparison would be to relate the inhibition of healing to the degree of anesthesia produced. Determination of the anesthetic properties of the several drugs lies outside the province of this study, however, tests were made on the intact human cornea in which the duration of anesthesia produced by these drugs under standard conditions was compared. Although the tests were preliminary in nature, they showed that the more dilute aqueous solutions used on the rats produced corneal anesthesia of short duration. Anesthesia following a one minute contact with a 0.5 per cent solution of phenacaine hydrochloride or butacaine sulfate persisted fifteen to twenty minutes, and that produced by 0.1 per cent nupercaine hydrochloride or 0.25 per cent tetracaine hydrochloride lasted twenty-five to thirty minutes. There was not a good correlation, therefore, between duration of anesthesia and inhibition of cell migration, for butacaine produced much delay in healing with a short period of anesthesia, whereas tetracaine gave a longer period of anesthesia with about the same delay in cell migration. However, the data on duration of anesthesia are few and were obtained from another species and on an intact rather than a broken epithelium.

The experiments with anesthetics in an ointment base clearly demonstrated that duration of anesthesia had no relation to the inhibition of healing. Figures 2 and 4 show that ointments containing an anesthetic had a far less deleterious effect on cell division and cell migration in the burned cornea than did aqueous solutions of the same drugs. These ointments also produced anesthesia which persisted far longer (one and a half to two hours) than did that produced by the aqueous solutions. It seems probable therefore (always assuming a similarity of anesthetic effect between rat and man) that the burned eyes were under anesthesia during the entire period of wound healing after the first application of the ointment without any appreciable slowing down of cell migration and, except for butacaine, without inhibition of mitosis. The fat-soluble anesthetics butyl aminobenzoate and orthoform in ointments both inhibited cell division and migration, the latter effect was greater with orthoform, whereas butyl aminobenzoate

<sup>12</sup> Michaelis, M., and Quastel, J. H. The Site of Action of Narcotics in Respiratory Processes, *Biochem J* 35 518, 1941.

<sup>13</sup> Herrmann, H., Moses, S. G., and Friedenwald, J. S. Influence of Pontocaine Hydrochloride and Chlorobutanol on Respiration and Glycolysis of Cornea, *Arch Ophth* 28 652 (Oct) 1942.

produced anesthesia of greater duration. From these experiments it seems clear that anesthesia is compatible with an almost normal rate of healing both in the cell division and in the cell migration phase. The reason for the superiority of ointments over aqueous solutions in this respect is not clear, however, the epithelial cells bathed in an aqueous solution of an anesthetic endure a very high concentration of the drug for a rather short time. The ointments may be presumed to release their drug rather slowly over a more extended period, so that the concentration of the anesthetic may not reach toxic levels at any time.

#### SUMMARY OF RESULTS

1 Topical application of most anesthetics inhibits mitosis in the intact corneal epithelium when concentrations which produce anesthesia are used.

2 The inhibition of cell division varies with different drugs, the method of administration and the frequency of application.

3 Anesthetics applied locally to corneal burns markedly inhibit the migration of epithelial cells over the injured area.

4 Cell division in the regenerating epithelium is also inhibited by most anesthetics.

5 The processes of cell migration and cell division are affected differentially. Cell migration may be notably retarded with little or no inhibition of cell division. Other drugs inhibit mitosis but do not markedly retard cell migration.

6 Some anesthetics (nupercaine and phenacaine ointments) can be used which produce prolonged surface anesthesia and which do not impair mitosis in the normal, or retard cell division or migration in regenerating, corneal epithelium.

7 Unbuffered aqueous solutions inhibit the healing processes far more than ointments of the same or greater strength, which produce anesthesia of longer duration.

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# STANDARD ILLUMINANTS IN RELATION TO COLOR-TESTING PROCEDURES

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## THE PROBLEM

What is wrong with the present color-testing procedures? Why do examiners often fail to expose persons with defective color vision? Does the fault lie in the tests, the methods of administering them or the conditions under which they are administered?

## IMPORTANCE OF THE PROBLEM

*In the Army*—An officer is shot because a cadet pilot fails to recognize a colored signal and fires an extra round. A bomber is shot down because a returning pilot fails to respond to a prearranged color signal code. Data of the Civil Aeronautics Administration show that a pilot who failed to pass the Ishihara test on the first attempt has a 50 per cent chance of passing a retest.

*In the Navy*—Tests conducted by members of the Committee on Color Blindness of the Inter-Society Color Council show that all the commonly used tests for color blindness are unreliable and largely ineffective as they are ordinarily administered.

*In Industry*—Because the wrong illuminant was used in making color matches, \$50,000 worth of silk is ruined. Because of faulty judgment of color, 100,000 pounds (50,000 Kg) of cotton is graded down.

A sheet metal printer in one instance lost the time and material for more than 780,000 talcum cans on which the color went wrong because some of the work was done under ordinary artificial light.

A lithographer was refused acceptance on a million calendars with a trademark design because the color, which appeared similar to the approved copy sheet under artificial light, was quite different and unsatisfactory in daylight. These calendars were worth only their weight in scrap paper.<sup>1</sup>

Physicians, especially ophthalmologists, should be interested in this problem, for it is their function to carry out these tests for color blind-

ness or defective color vision. Yet few ophthalmologists have any adequate understanding of the principles underlying tests for color vision or of safeguards essential to their administration. This is due partly to lack of training and to the fact that defective color vision is an anomaly, and not a clinical disease.

Any test of color vision involves three equally important factors: (1) the illuminant to be used, (2) the subject to be tested, and (3) the test and its proper administration.

In such a situation any one of the factors may be tested if, and only if, the other two are standardized or constant. Yet it is the rule rather than the exception to leave two of the factors (1 and 2) variable and thus hopelessly muddle any results obtained. The light (factor 1) is an instrument to be used in order to enable the subject (factor 2) to perform a certain task (factor 3). It is obvious that if on one occasion the subject is given a wretched instrument and on another occasion he is given a perfect instrument, he will perform differently on the two tests. At county fairs one tests one's strength by striking a blow on one end of a lever, the other end of which drives a ball up a guide wire. Other things being equal, it is obviously no test of strength if one man is given a tack hammer and the next man a sledge hammer. Considering the fact that color vision tests have been given to hundreds of millions of subjects, a fantastic amount of time and effort has been wasted through ignorance or disregard of this simple fact. It is established that by far the greater amount of work on color vision testing has been futile and invalid. Dimmick<sup>2</sup> has recently pointed out again that tests involving reflected light are "dependent for precision on the illuminant used."

Color vision tests are deliberately designed to be tricky and critical. The more critical they are the more accurate they are, but the more carefully must they be administered, and this

<sup>1</sup> Gage, H. P., and Macbeth, N. Filters for Artificial Daylighting. Their Grading and Use, *Trans. Illum. Engin. Soc.* **31** 995, 1936.

<sup>2</sup> Dimmick, F. L. Methodology in Test Preparation, *Am. J. Optom.* **20** 430, 1943.

means that more care must be used in selecting the illuminant used and in administering the test

Most color vision tests as presently administered are not tests for defective color vision but tests for lighting systems. It is easier to test factor 1 (the illuminant) than to test factor 2 (the subject), and this is what is commonly done. Excellent tests, using metameric colors, are now available for testing illuminants, but ordinary tests intended to evaluate color vision are usually—although unwittingly and erroneously—so administered that they test primarily the illuminant.

If some one is seen to place something on the pan of a spring scale and observe the position of the indicator, what is the inference? The answer depends on a fuller knowledge of the purpose and conditions of the procedure. If it is the first session of a high school physics class, one may be seeing tested the ability of the student to read a vernier, if it is in a grocery store, one is probably seeing a mass of spinach being weighed, however, if the scene takes place at the Bureau of Standards one is more likely seeing a set of scales being tested. But in testing color vision one always, unfortunately, assumes that it is spinach.

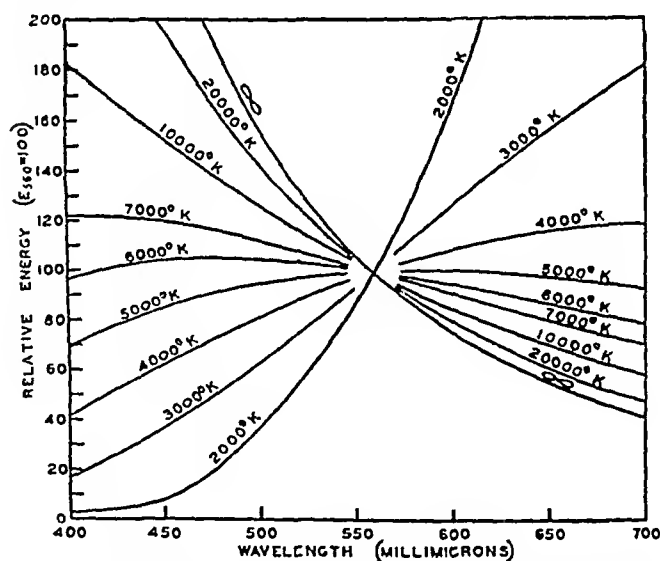


Fig 1—Relative distribution of energy in the radiation from a black body at various temperatures

Even the pseudoscientific who always use "daylight" fall into this error, for their "10 foot candle daylight," as will be shown, varies from candlelight to light much bluer than average north skylight. The stage has been passed where anything which comes in through a window can scientifically be called "daylight illumination." Properly administered, practically all color tests using reflected light are independent of the amount of illumination between 10 and 60 foot candles.

## BLACK BODIES AND APPARENT COLOR TEMPERATURE

Incandescent gases radiate line spectrums. In solids the atoms are so closely packed that they cannot emit radiations in a characteristic manner, as a result, a continuous spectrum is emitted. The emission is practically independent of the composition of the solid but depends primarily on its temperature. A black body is the perfect radiator. Such a radiator cannot

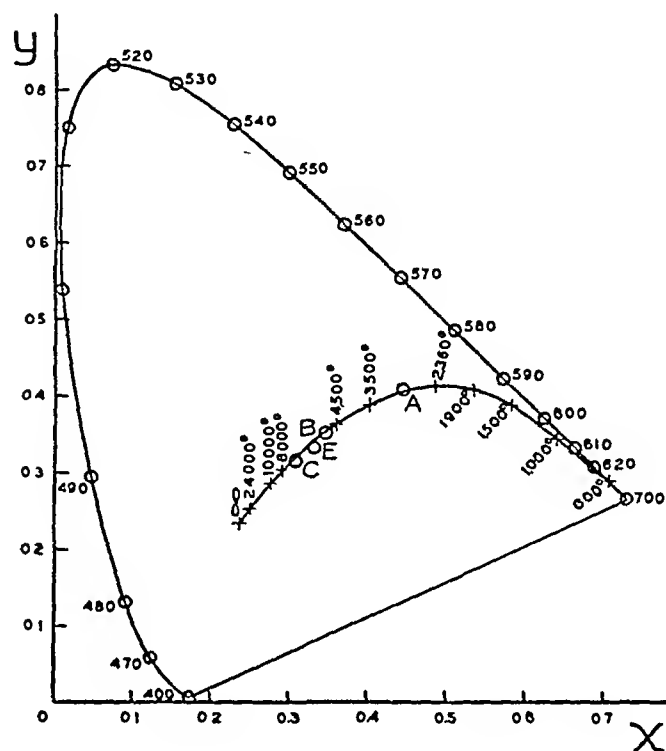


Fig 2—Chromaticities of various important illuminants. The solid line is the locus of radiation from a black body at various temperatures. The points A, B and C represent the chromaticity of the I C I illuminants. The point E represents the chromaticity of a source radiating equal amounts of energy in each wavelength interval.

be achieved in actual practice, but a small hole in a large sphere whose walls are maintained at a constant temperature furnishes a close approximation.

If such a body is heated, it will emit infra-red radiations, and as the temperature is increased, it will become visibly "red hot." With further increases in temperature it becomes "yellow hot," then "white hot" and finally, theoretically, "blue hot." "Blue hotness" cannot be achieved experimentally because all known materials evaporate long before this temperature is reached.

However, measuring the distribution of the energy radiated by a black body at various wavelengths and different temperatures gives a series of curves which can be plotted as distribution curves on simple graph paper (ordinates represent relative energy emitted, abscissas, wavelengths) or reduced to points on a color diagram.

Such scales are shown in figures 1 and 2, taken from Hardy,<sup>3</sup> and figure 3, from Macbeth<sup>4</sup>

From figure 3 it is seen that the sun seventeen minutes after sunrise or before sunset has the color temperature of a candle (1,900° K). A tungsten vacuum type lamp has a color temperature of about 2,400° K, a 100 watt, gas-filled Mazda C lamp, a color temperature of about 2,700° K, and a 200 watt Mazda C lamp, a color temperature of about 2,850° K. Noon sunlight at Washington, D. C., is only slightly yellowish, and its color temperature is a little above

light" as expressing "what comes in through the window" has no significance and is largely pseudoscientific self delusion

#### THE I C I STANDARD ILLUMINANTS

There have been for the past thirteen years a set of international standard illuminants precisely specified and capable of accurate reproduction. These illuminants were accepted and recommended for any work in color by the International Commission on Illumination, hence they are known as the I C I illuminants, sometimes

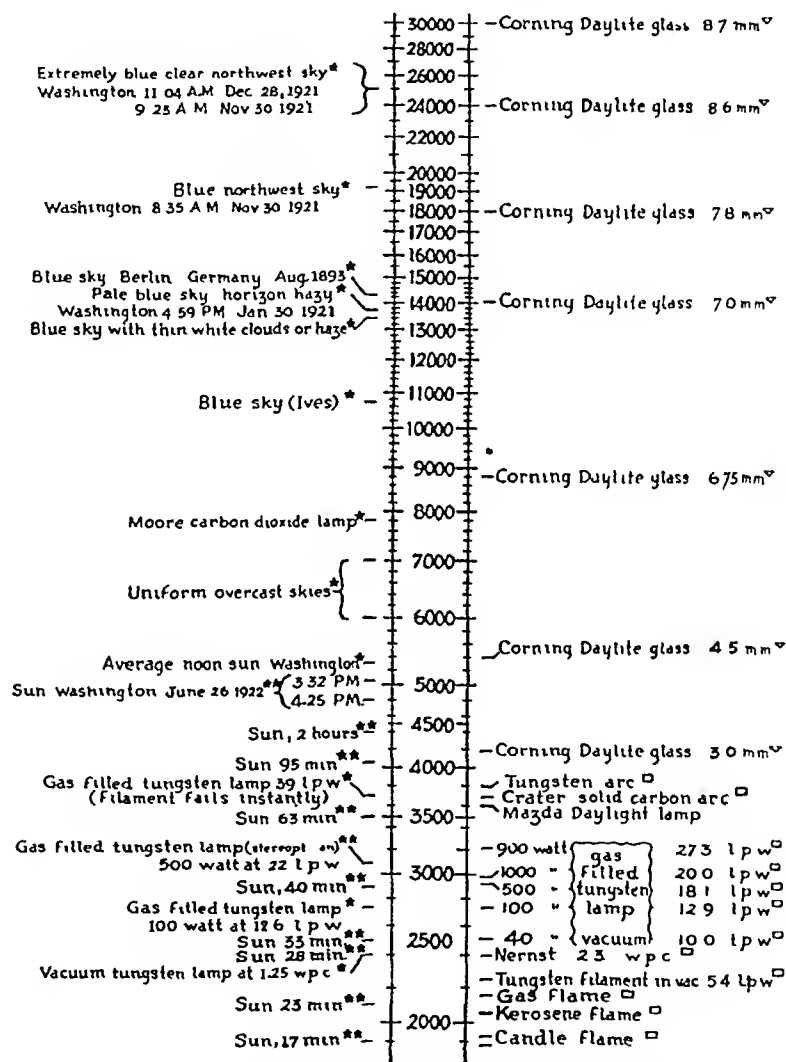


Fig 3—Sunlight, daylight and artificial light on the color temperature scale (from Macbeth,<sup>4</sup> page 302). Data marked by \*\* indicate direct sunlight, time after sunrise and before sunset. In this chart, data marked by the \* and \*\* were furnished by Priest, and those marked with a rectangle, by Cady and Dates, the data marked with an inverted triangle were obtained with a light source at 2898° K.

5,000° K. Uniform overcast skylight (6,000° to 7,000° K) is an important illuminant, and the color temperature of blue northwest clear skylight may run up to 25,000° K. Hence "day-

3 Hardy, A. C. Handbook of Colorimetry, Cambridge, Mass., Massachusetts Institute of Technology, 1936.

4 Macbeth, N. Color Temperature Classification of Natural and Artificial Illuminants, Tr. Illum. Engin. Soc., 23:302, 1928.

called C I E (*Commission Internationale de l'Éclairement*) illuminants. Sufficient time has elapsed and sufficient experimental and theoretic data have been produced to guarantee that the recommendations made in 1931 will serve for many years to come.

There are three recommended I C I illuminants. They are called I C I standard illuminants A, B and C. The official report of the

recommendations was published by Smith and Guild<sup>5</sup> and was summarized for American readers by Judd<sup>6</sup> in the *Journal of the Optical Society of America*, from which the following quotation is taken

It is recommended that the following three illuminants be adopted as standards for the general colorimetry of materials

A A gas-filled lamp of color temperature 2848°K

B The same lamp used in combination with a filter composed of a layer one centimeter thick of each of two solutions  $B_1$  and  $B_2$ , contained in a double cell made of colorless optical glass. The two solutions are made up as follows

*Solution  $B_1$*

Copper sulphate ( $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ )	2 452 g
Mannite ( $\text{C}_6\text{H}_8(\text{OH})_6$ )	2 452 g
Pyridine ( $\text{C}_5\text{H}_5\text{N}$ )	30 0 cc
Distilled water to make	1000 cc

*Solution  $B_2$*

Cobalt ammonium sulphate ( $\text{CoSO}_4 \cdot (\text{NH}_4)_2\text{SO}_4 \cdot 6\text{H}_2\text{O}$ )	21 71 g
Copper sulphate ( $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ )	16 11 g
Sulphuric acid (density 1 835)	10 0 cc
Distilled water to make	1000 cc

C The same lamp used in combination with a filter consisting of a layer one centimeter thick of each of two solutions,  $C_1$  and  $C_2$ , contained in a double cell made of colorless optical glass. The two solutions are made up as follows

*Solution  $C_1$*

Copper sulphate ( $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ )	3 412 g
Mannite ( $\text{C}_6\text{H}_8(\text{OH})_6$ )	3 412 g
Pyridine ( $\text{C}_5\text{H}_5\text{N}$ )	30 0 cc
Distilled water to make	1000 cc

*Solution  $C_2$*

Cobalt ammonium sulphate ( $\text{CoSO}_4 \cdot (\text{NH}_4)_2\text{SO}_4 \cdot 6\text{H}_2\text{O}$ )	30 580 g
Copper sulphate ( $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ )	22 520 g
Sulphuric acid (density 1 835)	10 0 cc
Distilled water to make	1000 cc

It is recognized that for certain special applications (for example, the specification of signal glasses) other luminous sources may be prescribed, but in the absence of special conditions one of the three indicated sources should be used

The liquid filter specified under illuminant B is the Davis-Gibson filter for converting color temperature 2848 to 4800°K, and that specified under illuminant C is the Davis-Gibson filter for converting 2848 to 6500°K. Illuminant A is intended to be typical of light from the gas-filled incandescent lamp, illuminant B is an approximate representation of noon sunlight, and illuminant C is an approximate representation of average daylight

It is to be noted that I C I illuminant A alone can be achieved from an unfiltered light source. Suitable I C I A lamps that have been

seasoned and calibrated may be obtained from the Bureau of Standards of the United States Department of Commerce and elsewhere. I C I illuminant A can be taken as a standard for indoor Mazda lighting

I C I illuminant B has the same source as I C I illuminant A, but the spectral energy distribution is modified by a filter. The exact specification requires two liquid filters, but these are necessary only for precise work. Glass filters are available which may be used in most practical circumstances to give a good approximation to I C I illuminant B, which can be considered a standard for white light or sunlight

Similarly close approximations to I C I illuminant C, which may be considered as standard daylight, can be achieved by means of lamp and glass filter combinations,<sup>7</sup> which have the apparent color temperature of a black body at about 6,700°K. Unless otherwise specified, this is the illuminant that should be used in all color testing involving the use of yarns, plates, chips, etc

Practically all color vision tests involving the use of reflected light were designed to be used under illumination approximating that given by I C I illuminant C, and to employ them under other conditions not only invalidates the test but yields misleading results. The use of Mazda light in administering such tests as the Ishihara, the Stilling, the American Optical Company and the Rabkin plates and the plates prepared at the Knapp Memorial Laboratories of the Institute of Ophthalmology not only fails to trap but actually assists the escape from detection, particularly of deuteranomalous and mildly protanomalous subjects. Similar results have been found by the Navy Department.<sup>8</sup> It were better not to give the test than to give it under conditions which almost inevitably mislead

## SUMMARY

Tests for defective color vision always involve three factors: the light used to see with, the subject tested and the materials and procedures of the test. Failure to standardize two of the three factors causes invalid results in evaluating the third factor. Most color vision testing is carried out under conditions which make the procedure

<sup>5</sup> Smith, T., and Guild, J. The C I E Colorimetric Standards and Their Use, *Tr Am Optic Soc* **33**:5, 1931-1932

<sup>6</sup> Judd, D. B. The 1931 I C I Standard Observer and Coordinate System for Colorimetry, *J Optic Soc America* **23** 359, 1933

<sup>7</sup> The filters may be obtained from Corning Glass Works, the lamp and filter combinations, from the Macbeth Daylighting Company

<sup>8</sup> Reed, J. D. The Effect of Illumination in Changing the Stimuli in Pseudo-Isochromatic Plates, *J Optic Soc America* **34**:350, 1944



as much a test of the illumination as of the subject's color discriminatory ability

Standard illuminants for testing are available and must be used if reproducible results are to be obtained

The illuminant must be an integral part of every accurate test

I C I illuminant C is the choice for all work in color vision testing which involves the use

of reflected light and, unless special conditions are indicated, should always be used. A sufficiently close approximation to this illuminant is commercially available at relatively low cost

Attention to this factor will enormously reduce the errors and misinterpretations now so prevalent in color vision testing

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# SENILE HYALINE SCLERAL PLAQUES

KENNETH L. ROPER, M D

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The recent literature describes two new lesions of the sclera—one primarily necrotic in origin and the other primarily degenerative in character

Within a period of six months I have observed 5 cases of the latter type. The condition is one of symmetric hyaline degeneration of the sclera, occurring in advanced age and characterized by the presence of slate gray plaques, situated about 3 mm from the limbus and 1.5 to 2 mm anterior to the insertions of the rectus muscles, to which they bear a definite relationship

Clinically, these hyaline areas probably escape notice because the patient rarely draws the physician's attention to their presence. I believe that they would be found much more frequently if ophthalmologists paid more attention to such conditions during their routine clinical examinations. It is surprising that so few contributions to the literature on the subject have been made

## REVIEW OF LITERATURE

I have made what I believe to be a complete review of the literature on the subject

Parsons<sup>1</sup> mentioned hyaline degeneration of the sclera, stating that "hyaline degeneration of the scleral laminae is found under pinguecula, and in other degenerative conditions." He also mentioned fatty degeneration and calcification of the sclera, occurring in advanced age after old inflammatory conditions

Salzmann<sup>2</sup> mentioned only a fatty degeneration which becomes apparent over the entire tunica fibrosa in old age, manifested on the cornea as arcus senilis, and which causes the sclera to change from a pure white to a yellowish tint. The sclera in old age, he said, becomes generally thickened, more rigid and less elastic

From the Dartmouth Eye Institute, Dartmouth Medical School, Hanover, N H

1 Parsons, J H. *The Pathology of the Eye*, London, Hodder & Stoughton, 1904, vol 1, pt 1, p 279

2 Salzmann, M. *Anatomie und Histologie des menschlichen Augapfels in Normalzustande, seine Entwicklung und sein Altern*, Vienna, F Deuticke, 1912

Rolandi<sup>3</sup> reported 3 cases in 1915, in all of which symmetric changes occurred in the sclera of both eyes. He stated that so far as he knew nothing similar had ever previously been described. In a 76 year old woman, he observed two slate gray spots on each eye, situated between the limbus and the insertions of the external and internal rectus muscles. The spots were semitransparent, nearly glassy, and measured about 5 mm vertically and 2 mm horizontally. He could see the fibrous structure of the tendon of the right external rectus muscle through the thin conjunctiva, as well as the insertion of the muscle itself. He attempted to remove a small piece from one of the spots by means of a trephine through an incision in the conjunctiva but was unsuccessful. He said that the trephine met with considerable resistance. Soon after he observed the condition in his first patient, he noted a similar spot on the nasal side of one eye in a 72 year old patient and two large spots on the nasal side of both eyes in a 77 year old patient. Rolandi believed the condition to be a degenerative process. He felt that the slate gray spots were due to mechanical factors, that there followed a transformation of the fibrous tissues of the sclera into cartilage and that the cartilage later degenerated into hyalin, which permitted the pigment of the choroid to shimmer through. He noted the following characteristics with regard to the spots: their elective position, rectangular shape, slate gray color, semitransparency and nearly osseous consistency. Rolandi accompanied his article with photographs which present the same characteristics as those in my cases and in the cases reported in the literature which are cited here

Krekeler,<sup>4</sup> in describing the structure of the sclera at various periods of life, stated that in advanced age the elastic fibers, especially in the middle layers of the sclera, and the number of

3 Rolandi, S. *Sulla presenza di speciali chiazze nella sclera di probabile natura cartilaginea*, *Ann di ottal* 44 843-857, 1915

4 Krekeler, F. *Die Struktur der Sklera in den verschiedenen Lebensaltern*, *Arch f Augenh* 93.144-159, 1923

scleral fibers themselves decrease and that there are deposits of fat globules and lime

Pillat<sup>5</sup> described, in 1933, a peculiar senile degeneration of the sclera which he had observed in an 88 year old woman. He noted two dark vertical spots in each eye, in front of the insertions of the external and internal rectus muscles. He was also able to see the tendons of the muscles themselves, shining through the thin conjunctiva. Pillat was evidently familiar with the experiments of Fischer,<sup>6</sup> who had observed similar spots in subluxated rabbit eyes, and concluded that the semitransparency and thinness of the sclera in the affected areas were due to loss of the water content of the sclera. Knowing that the entrance of the tendon fibers into the sclera continually expose it to mechanical action, he surmised that the affected area was predisposed to give off more water to offset its mechanical vulnerability. Pillat was familiar with the cases reported by Rolandi but did not believe they were similar to his. He felt that the condition in Rolandi's cases was due to secondary scleral degeneration of some other origin.

Kiss<sup>7</sup> reported a case of senile thinning of the sclera before a session of the Ophthalmological Society in Vienna, on Oct 16, 1933. In an 86 year old patient he had observed bilateral slate-gray spots in the sclera, situated between the limbus and the insertion of the external rectus muscle. He regarded the condition as an early stage of senile degeneration and inferred that his case was similar to the one described by Pillat. He was sure that the condition was not rare, as he had observed 2 other cases within a few weeks.

Kreibitz,<sup>8</sup> in discussing the case reported by Kiss, stated that he had observed a number of patients with similar changes and that only the aged were affected.

Graves has written four times on the condition since 1936. In Berens' textbook, he<sup>9</sup> described a condition which at first glance suggested that a tenotomy of the internal rectus muscle had previously been performed because of a small, sharply defined area where the sclera was thinned.

5 Pillat, A. Ueber eine eigenartige senile Entartung der Lederhaut an den Ansatzstellen der geraden Augenmuskeln, *Ztschr f Augenh* **82** 113-123 (Dec) 1933

6 Fischer, F. P. Experimentelle Untersuchungen an der Lederhaut, *Arch f Augenh* **97** 467-492 (Dec) 1926

7 Kiss, J. Fall von seniler Skleraverdunnung, *Klin Monatsbl f Augenh* **92** 121-122 (Jan) 1934

8 Kreibitz, W., in discussion on Kiss,<sup>7</sup> p 122

9 Graves, B., in Berens, C. *The Eye and Its Diseases*, Philadelphia, W. B. Saunders Company, 1936, p 468

In 1937, he<sup>10</sup> reported in more detail on cases in which he had observed the condition. At that time he regarded the defects as developmental in character and stated he was not aware that such a condition had previously been reported.

In a later article, Graves<sup>11</sup> said that Ida Mann had questioned whether the defects he had noticed were developmental in character and had suggested that the condition might be due to a hyaline degeneration of the sclera, and not to structural thinning, as he had stated. In this article, Graves said that he had jumped to the conclusion, in the first few cases he had observed, that the condition was a developmental defect but that he was now in agreement with the conclusive and interesting histopathologic evidence described by Culler.<sup>12</sup> Up to this time Graves had observed the condition only on the mesial aspect of the sclera, whereas in the case he was now reporting there were not only mesial plaques but some evidence of lateral plaques.

Graves<sup>13</sup> reported a case in 1941 in which the plaques were seen only on the temporal aspect of each eye. He was now convinced that the condition was not necessarily confined to the mesial aspect of the sclera and agreed that the words "developmental" and "mesial" should be dropped. He felt that the term "scleral plaques" was quite suitable.

Urrets Zavalía and associates<sup>14</sup> described a case of the defect in a man aged 68, which was observed during the course of chronic porphyrinuria. Symmetric bilateral temporal lesions were present. A piece of the degenerative plaque in the left eye was removed for histologic study. The tissue was described as being similar to that of the sclera, but without cellular elements and with hyaline degeneration and calcification. It was felt that the term "scleromalacia" adequately described the condition and that the case was similar to the one described

10 Graves, B. Bilateral Mesial Superficial Deficiency of the Sclera, *Brit J Ophth* **21** 534-538 (Oct) 1937

11 Graves, B. Bilateral Mesial Superficial "Deficiency" of the Sclera (Scleral Plaques), *Brit J Ophth* **23** 191-204 (March) 1939

12 Culler, A. M. The Pathology of Scleral Plaques. Report of Five Cases of Degenerative Plaques in the Sclera Mesially, One Studied Histologically, *Brit J Ophth* **23** 44-50 (Jan) 1939

13 Graves, B. Bilateral (Mesial) Deficiency of the Sclera. Scleral Plaques, *Brit J Ophth* **25** 35-38 (Jan) 1941

14 Urrets Zavalía, A., Maldonado Allende, I., and Obregon Oliva, R. Scleromalacia Observed During the Course of a Chronic Porphyrinuria, *Arch de oftal de Buenos Aires* **12** 115-137 (March) 1937

by van der Hoeve,<sup>15</sup> for even though perforation had not occurred, it might logically be expected in the future. The authors wondered whether some relation might exist between the disturbance of the sclera they had observed in their patient and the chronic porphyrinuria, with its peculiar cutaneous lesions. They also wondered whether the ocular condition might have some relation to the curious anomaly of nutrition which was present in their patient. The case described by these authors was undoubtedly one of senile hyaline scleral plaques, and the accompanying chronic porphyrinuria and nutritional disturbances were purely coincidental.

Gasteiger,<sup>16</sup> in 1937, reported a case of senile degeneration of the sclera at the insertions of the rectus muscles in a 78 year old woman. The bandlike changes were noted both temporally and nasally in each eye. A narrow, horizontal band was seen in front of the insertion of the inferior rectus muscle in the right eye only. Gasteiger expressed agreement with Pillat that the condition was the result of dehydration and that the process first becomes conspicuous in the areas of the insertions of the muscles, as they are especially vulnerable to damage of this sort. By treating pigs' eyes with glycerin and alcohol, he produced dehydration, through fluid drainage, within a few minutes, but the condition of the eyes was normal after they emerged from water or a saline solution. He produced similar changes in the eyes of living rabbits. Under the influence of the normal tissue fluids, however, the sclera quickly reverted to its natural condition. Since Gasteiger was unable to make the bands in his patient's eyes disappear by touching them with salt or by irrigation, he concluded that, in addition to dehydration, there must be permanent changes in the tissues, which might be designated as a form of senile atrophy.

Rones,<sup>17</sup> in a comprehensive survey of senile changes in and degenerations of the eye, included the clinical entity described by van der Hoeve<sup>15</sup> of "degenerative hole-formation in the sclera without evidence of inflammation" but did not mention senile hyaline scleral plaques. He stated that senile changes of the sclera are characterized by fatty infiltration, frequent deposits of fine granules of calcium salts in the posterior segment and widening of the con-

nective tissue bundles with diminution in the number of nuclei. He stated, further, that degeneration of elastic tissue occurs, that the vessels become surrounded by fat droplets and that the arteries particularly show evidence of sclerosis. Rones stated, further, that the sclera is not frequently involved in degenerative changes of old age and that occasionally calcification, rarely bone formation, associated with inflammatory symptoms, is seen.

Culler<sup>12</sup> reported 5 cases of scleral plaques in 1939. All of the lesions in his cases were located mesially. He was able to obtain a specimen at autopsy in 1 of his cases and described the histologic appearance as clearly a degenerative change, involving large masses of hyalin. He permitted me to study six excellent Kodachrome slides illustrating his cases. The clinical appearance of the plaques in his cases was identical with that of the plaques in my cases.

Kyrieleis,<sup>18</sup> in 1939, reported certain changes of the sclera in 3 patients of advanced age. A 77 year old man, who had had one eye enucleated, showed a thinning of the sclera of the other eye both nasally and temporally, not far from the limbus, through which the uvea was discernible. A second patient, aged 70, presented the same type of scleral thinning in both eyes, but only on the nasal side. In the third patient, a 60 year old man, the lesions were bilateral and were seen nasally as well as temporally. Kyrieleis had the opportunity to study the enucleated eye of his first patient. The eye had been removed because of absolute glaucoma due to a melanosarcoma of the choroid. Scleral lesions were present in this eye and appeared much like those in the remaining eye. Histologic examination showed degeneration of the superficial fibers of the sclera and pronounced calcification. Kyrieleis acknowledged that the histologic picture was complicated by the fact that the specimen came from a glaucomatous eye, at the same time, he pointed out that in the case described by Urrets Zavalía and associates<sup>14</sup> some calcification, in addition to hyaline degeneration, was present. While Kyrieleis regarded the lesion he had observed as circumscribed degeneration of the sclera (scleromalacia), he expressed doubt that it was basically different from the lesion known as scleromalacia perforans. He stated the opinion that the calcium plaques within the scleral tissue were virtually sequestered and would eventually perforate, thus reaching the stage of the condition described by

15 van der Hoeve, J. Scleromalacia Perforans, *Arch Ophth* 11:111-118 (Jan) 1934.

16 Gasteiger, H. Ueber senile Entartung der Lederhaut an den Ansatzstellen der Augenmuskeln, *Klin Monatsbl f Augenh* 98:767-772 (June) 1937.

17 Rones, B. Senile Changes and Degenerations of the Human Eye, *Am J Ophth* 21:239-255 (March) 1938.

18 Kyrieleis, W. Ueber umschriebenen Lederhautschwund (Skleromalazie) in hoherem Lebensalter, *Klin Monatsbl f Augenh* 103:441-452 (Oct-Nov) 1939.

van der Hoeve<sup>15</sup> He also called attention to the fact that in his cases and in the case described by Urrets Zavalía and associates the spots were regularly located, while in other cases of scleromalacia reported the areas were scattered indiscriminately

Summarizing the studies made on his own patients, Kyrieleis stated that clinically the lesions appeared as degenerative changes in the sclera They were located between the insertions of the horizontal rectus muscles and the limbus He was unable to ascertain in any of his cases when the areas first appeared In none of his cases had the lesion reached the stage of perforation Two of his patients had an associated arthritic condition, and he inferred that rheumatic disease favored the development of the scleral defects He also stated the belief that senile changes of metabolism and of the blood vessels were significant

Duke-Elder<sup>19</sup> made no mention of senile hyaline scleral plaques in his textbook, although he specifically mentioned the condition recently described by van der Hoeve<sup>15</sup> as "scleromalacia perforans" Duke-Elder stated that degenerative changes are not uncommon in the sclera and that fatty degeneration is usual in old age, the process giving the sclera a yellowish color He stated that calcification occurs not uncommonly both as a senile degeneration and as a terminal event in postinflammatory fibrosis As for hyaline degeneration, he merely stated that it is almost universally found in old age, in the tissues under a pinguecula, as a sequel to inflammation and by extension from the subconjunctival tissues Senile hyaline scleral plaques can hardly be included under such a description

Von Bürki,<sup>20</sup> in his review of diseases of the sclera, mentioned the cases of senile degeneration of the sclera described by Gasteiger,<sup>16</sup> Culler<sup>12</sup> and Graves<sup>21</sup>

Boshoff,<sup>22</sup> in 1942, described observations in 11 cases of scleral plaques and discussed the literature He gave credit to Pillat<sup>5</sup> for having given the first full description of the condition and to Culler<sup>12</sup> for the first histologic description of scleral plaques

I have already brought out in this review that Rolandi,<sup>3</sup> eighteen years before Pillat, described degenerative changes in the sclera of the eyes of 13 patients, both eyes being affected in each

case He accompanied his description with photographs clearly showing that the condition was identical with that in the cases described here Pillat himself was familiar with the cases reported by Rolandi, but, as I have said before, he did not believe that the defects were of the same nature as the lesions in his cases I have also shown that Urrets Zavalía and associates,<sup>14</sup> two years before Culler,<sup>12</sup> reported histologic studies in a case of scleral plaques

Although only 4 of his 11 patients had arthritis, Boshoff<sup>22</sup> stated that there seemed to be a definite connection between polyarthritic disease and scleral hyaline plaques He was unable to discover any other constitutional dyscrasia which might have had an influence on the formation of the plaques Boshoff supported Culler<sup>12</sup> and Graves in their choice of the name "scleral plaques," which he said described the essential nature of the condition He<sup>22</sup> mentioned in a footnote that Ascher described the condition at an ophthalmologic congress in Vienna at about the same time as Pillat Ascher<sup>23</sup> does not recall the exact date of his discussion mentioned by Boshoff and makes no claim to priority in describing the condition He became interested in these scleral spots after learning of the experiments of Kahn and Fischer<sup>6</sup> He expressed the belief that there might be some connection between these experiments on dehydration and the scleral spots of hyalinization Ascher states that he rarely saw these scleral spots in Prague but that he has observed them more frequently in this country He observed 4 patients in the nutrition clinic at Birmingham, Ala., all of whom had nicotinic acid deficiency, which in 1 patient was combined with a deficiency in riboflavin and thiamine Ascher raises the question whether such deficiencies or the hot climate or both may have some influence on the development of the scleral hyaline spots He has never observed such a spot in relation to the superior rectus muscle and offers the explanation that this part of the sclera is constantly covered by the upper lid and protected against noxious factors, one of them possibly being exsiccation Ascher also points out that the fibers of the tendons of both the external and the internal rectus muscle are visible with oblique illumination but are still clearer with the corneal microscope

#### ANATOMIC AND PHYSIOLOGIC CHARACTERISTICS OF THE SCLERA

*An understanding of the structure and physiologic activity of the sclera enables one to appreciate how ideally it is protected against the*

19 Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1940, vol. 2, p. 2065

20 von Bürki, E. *Cornea, Episklera, Sklera*, *Ophthalmologica* **103** 405-420, 1942

21 Graves (footnotes 9, 10, 11 and 13)

22 Boshoff, P. H. *Hyaline Scleral Plaques*, *Arch Ophth* **28** 503-506 (Sept.) 1942

23 Ascher, K. W. Personal communication to the author

invasion of micro-organisms and yet how peculiarly defenseless it is to repel infection or to combat influences making for degeneration

The sclera consists of fibrils of connective tissue united into bundles, resembling the lamellas of the cornea but less regular and more firmly packed. The bundles run chiefly in two directions, meridionally and equatorially. There are also many oblique bundles. The entire arrangement is interrupted by the entrance of the tendons of the extraocular muscles. A large number of extremely fine elastic fibers are scattered throughout. They are fewer in youth. The outer layers of the sclera contain more elastic fibers than the inner, and the fibers are more numerous posteriorly than anteriorly. Between the bundles of fibers are lymph spaces, containing fixed connective tissue cells, though these are far less numerous than in the cornea. The inner surface of the sclera is normally pigmented and forms the lamina fusca. It is united with the choroid by fibrils of pigmented connective tissue and is lined with endothelial cells, thus forming the external wall of the suprachoroidal lymph space. The outer surface of the sclera is also covered with a single layer of endothelial cells.

The sclera, being composed almost entirely of fibrous and elastic tissue and with merely a protective function to perform, carries on a very low grade of metabolic activity and is therefore poorly vascularized. The blood vessels and nerves of the sclera are few. Arteries are given off from the short posterior and anterior ciliary vessels. The posterior ciliary veins—smaller than the corresponding arteries—are derived entirely from the sclera, the anterior ciliary veins only in part. The blood vessels form a network almost entirely confined to the episcleral tissues. This network is extremely attenuated except in the anterior region near the corneal margin. The close capillary system here may be seen clinically in inflammatory conditions as it enters into the picture of a ciliary injection.

The nerve supply of the sclera is scant and is derived from the posterior ciliary nerves as they run between the sclera and the choroid.

The scarcity of blood supply in the sclera accounts in part for the slow healing of scleral wounds. The extraordinarily low regenerative ability of scleral tissue, which is partly due to the scarcity of blood in the sclera, has great practical significance in ocular surgical procedures involving the sclera. The results of trephining operations on the sclera for the purpose of lowering the intraocular tension in cases of glaucoma are determined by this factor. When filtration ceases, it is not the result of scar formation but

is due to filling in of the opening by a substitute tissue, which is more compact than normal scleral tissue and which arises from the episclera and uvea—the sclera playing little part in its formation. The resulting scar has transparency but is not permeable to fluids.

The opaque white appearance of the sclera depends on its water content. Studies of the chemical composition of the sclera have shown that it contains a large percentage of water—over 65 per cent—while proteins make up the bulk of the solid matter.

Fischer<sup>6</sup> has shown that the fibers constitute a gel which combines reversibly with water, and that when the water content is at its normal level, it reflects the light diffusely so that it appears opaque. Fischer demonstrated that with a fluid content of 40 to 80 per cent the sclera of rabbits remained white, while with an increase or decrease of fluid content it became semitransparent.

Fischer credited Kahn with first observing the appearance of rectangular spots in the region of the insertion of the rectus muscles in subluxated rabbit eyes. Fischer proved that the spots thus produced are the result of local dehydration, and are in no way produced by any changes in circulation, intraocular tension, undue stretching of ocular muscles or nervous factors, and that the phenomenon is reversible. He discovered that the phenomenon is not limited to such specific locations but can be produced over the entire sclera by the use of strong hygroscopic materials, and that it is also reversible for the entire sclera. He further proved that the sclera becomes transparent not only when it is dehydrated but when its fluid content is above normal. In histologic studies, Fischer observed only marked thinning of the sclera that had been dehydrated and so could give no explanation as to why transparency exists in the spots produced. The question is much the same as that which has so long fascinated histologists with reference to the cornea and its transparency. Although the experimental spots induced by Fischer disappeared on replacement of the globe, no local measure has been known to change in any manner the appearance of the spots observed in patients of advanced years.

#### ETIOLOGIC FACTORS

Advanced age is largely responsible for predisposition to the disease, since in the aged dehydration and progressive sclerosis of the connective tissue of the entire body, as well as of the external tunic of the eye, occur. It is probably the result of a local nutritional disturbance, which, in turn, is due to arteriosclerotic changes. Certainly, vascular changes must be of funda-



mental importance, since degeneration taken as a whole is the result of faulty circulation

The fact that this unusual degenerative condition of the sclera has a predilection for the area lying in front of the insertions of the rectus muscles leads one to the additional assumption that the changes occur not only because of local circulatory disturbances but because of the constant stress and strain on the scleral fibers which are in such close proximity to the insertions of the rectus muscles

Susceptible as the elderly are to some form of arthritis in peripheral joints, the spinal column or both, the presence of aggravated or pronounced arthritis in a patient with senile hyaline scleral plaques should not lead one to assume that the ocular lesion is essentially a part of the disease. I am not convinced of any definite connection between polyarthritic disease and senile hyaline scleral plaques. A rheumatic disorder might well aggravate an existing vasosclerotic condition and so be an indirect contributory factor. In reviewing nearly 50 cases reported in the literature, together with my own 5 cases, I have been unable to determine any single constitutional disease which, either directly or indirectly, influences the formation of the plaques

#### CLINICAL DESCRIPTION

Senile hyaline scleral plaques must be regarded as a clinical entity, although the condition is characterized by absence of clinical symptoms

The plaques are situated about 3 mm from the limbus and 1.5 mm to 2 mm anterior to the insertions of the rectus muscles. They are generally rectangular, but occasionally only a rounded or oval patch, situated opposite either end of the insertion of a rectus muscle, is observed. They are seen most commonly opposite the insertion of the internal rectus muscle but occur next in frequency opposite that of the external rectus muscle. Rarely have they been observed opposite the insertion of the inferior rectus muscle. In none of my cases, nor in any of the cases described in the literature, were plaques observed opposite the insertion of the superior rectus muscle. Their average width is 1.5 mm to 2 mm and their average length 5 mm to 6 mm. The patches are not elevated but appear somewhat depressed. The limbal margins in general are more sharply defined. The irregularity of the tendinous margins is probably due to the presence of the interwoven tendon fibers. The sclera does not appear to have lost any of its firmness, in fact, it seems to be even more rigid and resistant. On transillumination of the globe, the areas show as relatively clear and translucent windows

The spots do not correspond to the muscle insertion themselves but lie just ahead of them, favoring the insertions a little more than the limbal margins. In many instances, one is able to observe through the thin conjunctiva an individual muscle tendon and its insertion as well, the tendon ending in a perpendicular line close to the spot. The slight obliquity of the dark bands also conforms to the slightly oblique insertions of the horizontal rectus muscles. The length of the dark bands also corresponds fairly well to the width of the tendon insertions

There is no disturbance of the overlying conjunctiva. Episcleral and conjunctival blood vessels course normally over the patches except for occasional tortuosity in keeping with the vasosclerotic state of the patient

The slate gray discoloration has nothing to do with pigmentation of the sclera, the episclera or the bulbar conjunctiva. When the lesions are studied carefully with oblique illumination and a loupe or a slit lamp and corneal microscope, the dark discoloration is seen as a shining of the uveal pigment of the ciliary body through the semitransparent sclera in that area. Even with the naked eye one can see that the peculiar slate gray color bears no resemblance to the brownish yellow tint of a pigmentation

As far as I have been able to determine, the condition is not a hazard to the eye. When present, lowered visual acuity was due to changes either in the lens or in the fundus or to chronic glaucoma, not to the plaques

#### HISTOLOGIC DESCRIPTION

Histologic studies have shown that the condition is primarily degenerative. In place of normal sclera, there remain some cellular and nuclear fragments and large masses of hyalin. There is general atrophy of the overlying conjunctiva and episclera

Marked calcification was reported in 2 cases. In 1 instance (Kyrieleis<sup>18</sup>) the picture was complicated by the fact that the eye was glaucomatous. In the other, the patient was suffering with a curious anomaly of nutrition (Urrets Zavalía and associates<sup>14</sup>)

#### DIFFERENTIAL DIAGNOSIS

*Scleromalacia perforans*—A condition which bears no real resemblance, but which has been confused with it, is scleromalacia perforans. The two conditions are alike only in their chronicity and in the fact that they affect the sclera predominantly. Scleromalacia perforans is primarily necrotic in origin, whereas senile hyaline scleral plaques are primarily degenerative in character

Culler<sup>12</sup> questioned whether these scleral spots were not the early stage of scleromalacia perforans. Kyrieleis<sup>18</sup> expressed doubt that the condition in his 3 cases was basically different from scleromalacia perforans and stated the belief that the plaques would eventually perforate, thus reaching the stage of the condition described by van der Hoeve.<sup>15</sup> Urrets Zavalia and associates<sup>14</sup> applied only the term scleromalacia, predicting that in their case the patches would perforate later.

Verhoeff and King<sup>24</sup> evolved a description of the clinical course of scleromalacia perforans which distinguishes this condition from that of senile hyaline scleral plaques. Scleromalacia perforans starts with slightly elevated nodules, involving the sclera and the overlying tissue. These nodules may be situated anywhere between the corneal limbus and the equator. Definite evidence of rheumatoid arthritis exists at the onset of the scleritis. Necrotic processes follow, resulting in formation of a sequestrum, which becomes completely disintegrated and densely infiltrated with necrotic pus cells. A cavity results, due to perforation and discharge of the sequestrum.

In cases of senile hyaline scleral plaques, a history of any serious arthritis is lacking, nor is there a history of nodules on the sclera. The lesions have not been known to occur anywhere except between the insertions of the internal or the external rectus muscle and the inferior rectus muscle and the limbus, whereas scleromalacia perforans may occur anywhere in the sclera which is covered by conjunctiva.

*Brawny Scleritis*—While brawny scleritis affects the sclera predominantly and occurs in the advanced years of life, it differs greatly histologically from senile hyaline scleral plaques. In brawny scleritis there are an invasion of the anterior portion of the sclera and the tendons of the rectus muscles with granulation tissue richly infiltrated with plasma cells and a diffuse plasma cell infiltration of the ciliary body and the anterior part of the choroid (Verhoeff<sup>25</sup>).

*Blue Sclera*—Needless to say, blue sclera does not have to be differentiated from senile hyaline scleral plaques, which is a degenerative change, and not a developmental one.

*Sarcoma*—A senile hyaline scleral plaque must not be mistaken for a sarcoma, and enucleation should never be considered. Graves<sup>10</sup> men-

tioned that in 1 of his cases the patient had consulted him because she had been told that her eye was sarcomatous. On careful inspection of the defect, the clearcut appearance of senile hyaline scleral plaques does not suggest a disintegrating eruption from beneath. The slate gray color of the plaque, moreover, has nothing whatever to do with pigmentation.

#### REPORT OF CASES

**CASE 1**—Mrs W. C., aged 81, who was first seen on July 22, 1944, complained of blurred vision. Vision in the right eye had been poor since an attack of iritis and ulcers, fifteen years before. Vision in the left eye was satisfactory. The patient was able to read newspaper without a magnifying glass. There were no known chronic ailments. Corrected vision was 20/70—2 in the right eye and 20/40+2 in the left eye. An immature senile cortical cataract was present in the right eye and another, less advanced, in the left eye. The right fundus was blurred, arteriosclerotic changes with accompanying retinopathy were noted in the left eye. Examination with the slit lamp revealed evidence of old anterior uveitis in the right eye. Intraocular tension was 22 mm in the right eye and 25 mm in the left eye (Schiotz).

On the mesial aspect of each eye, slate gray plaques were noted. They were situated about 3 mm from the limbus and about 1.5 to 2 mm anterior to the insertion of the internal rectus muscle. Their average width was 2 mm and their length 5 to 6 mm (fig 1 A and B).

On the temporal aspect of each eye was seen a somewhat rounded, slate gray patch, situated between the insertion of the external rectus muscle and the limbus (fig 1 C and D).

While the patient and her daughter were both aware of these spots, they were unable to state when they had first noticed them. The oculist who had attended the patient for many years had observed the dark areas on the sclera but was also unable to state when he had first noticed them.

There was no disturbance of the overlying conjunctiva. On transillumination of the globe, the areas appeared as relatively clear, translucent windows. The several tortuous conjunctival vessels seen in each eye were in keeping with the age and vasosclerotic state of the patient.

The patches were not elevated but were somewhat depressed. The edges were more sharply defined along the corneal border. When they were viewed with oblique illumination and a loupe or a slit lamp and corneal microscope, it was clearly evident that the spots were not pigmented but were the result of thinning of the sclera itself. Beneath the glassy patches the uveal pigment of the ciliary body was visible.

**CASE 2**—Mr W. G., aged 78, was first seen on Oct 10, 1944. His poor vision in both eyes was due to chronic glaucoma of long standing. Visual acuity was 20/80 in the right eye and 20/200 in the left eye. The visual fields of both eyes were constricted, to within 10 degrees of fixation except for a narrow projection below to the 25 degree isopter. The tension in each eye averaged 19 to 25 mm (Schiotz). The patient was using 1 per cent pilocarpine nitrate three times a day. He had no chronic ailment and had always been exceptionally well.

24 Verhoeff, F. H., and King, M. J. Scleromalacia Perforans. Report of a Case in Which the Eye Was Examined Microscopically, *Arch Ophthalmol* 20:1013-1035 (Dec) 1938.

25 Verhoeff, F. H. Brawny Scleritis, *Ophthalmoscope* 11:2-10, 1913.



Fig 1—Case 1 *A*, mesial aspect of right eye, *B*, mesial aspect of left eye, *C*, temporal aspect of right eye; *D*, temporal aspect of left eye Case 3 *E*, mesial aspect of right eye, *F*, mesial aspect of left eye, *G*, temporal aspect of right eye, *H*, temporal aspect of left eye Case 4 *I*, mesial aspect of right eye, *J*, mesial aspect of left eye

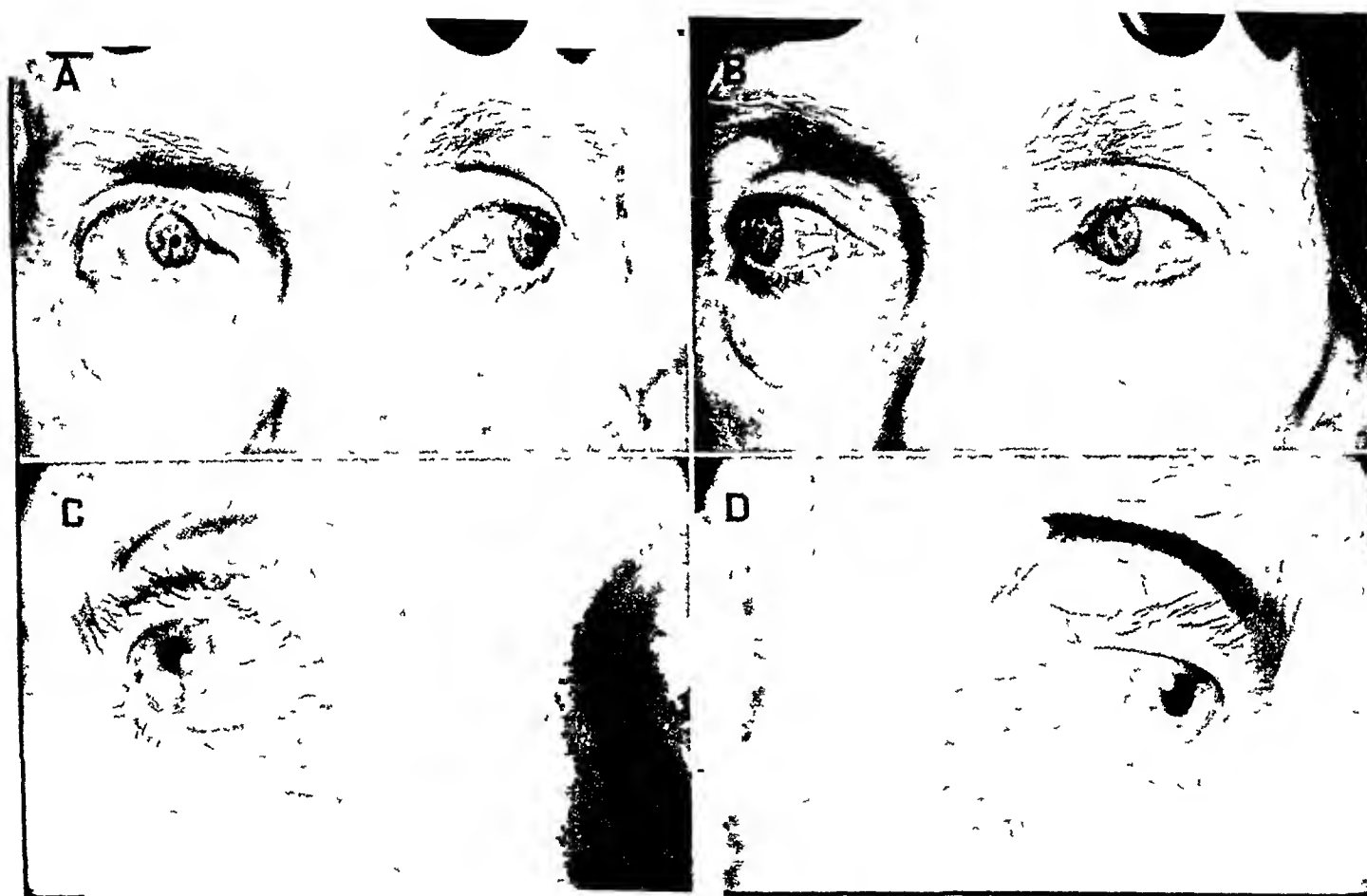


Fig 2—Case 3 *A*, patient looking to left, *B*, patient looking to right Case 4 *C*, mesial aspect of right eye, *D*, mesial aspect of left eye



Slate gray plaques were noted on both the mesial and the temporal aspect of each eye, they were most marked on the temporal aspect of the left eye and least marked on the nasal side of the right eye

CASE 3—Mrs F M, aged 72, was first seen on Nov 6, 1944. She complained of dryness and sticking of the lids, especially on retiring and on awakening in the morning. She had had an attack of arthritis in her left shoulder thirty years previously and a nasal operation and cholecystectomy in recent years. The refractive error was hyperopic astigmatism and presbyopia. Corrected vision was 20/20 in each eye.

When the patient's attention was called to the presence of the slate gray patches on both her eyes, she said that she had been aware of them for many years. The plaques were rectangular and were situated anterior to the insertions of the internal and external rectus muscles of each eye. The plaque on the lateral aspect of the right eye was 175 mm wide and 4 mm long, and the plaque on the mesial aspect measured approximately 2 by 35 mm. The plaque on the mesial aspect of the left eye measured 25 by 5 mm, and that on the lateral aspect, 1 by 3 mm (figs 1 E, F, G and H and 2 A and B).

The tendons of both external rectus muscles, and their insertions as well, were clearly visible through the conjunctiva. The insertions ended in perpendicular lines close to the plaques. The tendons and insertions of the internal rectus muscles could also be seen but were somewhat obscured by overlying conjunctival vessels.

CASE 4—Mrs M A, aged 88, was first seen on Nov 22, 1944. She complained of failing vision in both eyes for thirty-five years. For several years she had been using a magnifying glass for reading and had been seeing halos around lights. Her vision had seemed worse and the halos more pronounced during the past week. She was found to have moderate hypertension and auricular fibrillation. She had been troubled with arthritis of the left knee for the past ten years.

Visual acuity was 20/400 in each eye and was not improved with glasses. The patient had an immature senile nuclear cataract and senile macular degeneration in each eye. The intraocular tension was 21 mm in the right eye and 19 mm in the left eye (Schiotz).

A slate gray plaque was noted on the mesial aspect of each eye (figs 1 I and J and 2 C and D). Each plaque was situated about 3 mm from the limbus and anterior to the insertion of the internal rectus muscle. The patient was not aware of their presence.

CASE 5—Mrs E F, aged 72, was first seen on Dec 6, 1944. She complained of failing vision in both eyes. She had a high degree of myopia and had worn glasses since 11 years of age. She had been aware of spots on the inner side of each eye for several years. Her general health was good.

Corrected vision was 20/25—2 in the right eye and 20/200 in the left eye. Myopic choroiditis was present in both eyes.

Slate gray plaques were noted on both the mesial and the temporal aspect of each eye. The plaque on the mesial aspect of the right eye measured approximately 15 by 4 mm. Only a rounded patch was noted on the mesial aspect of the left eye. It was situated opposite the lower end of the insertion of the left internal rectus muscle.

Rounded patches were faintly visible on the temporal aspect of each eye, opposite the insertion of the external rectus muscle. The fibers of the external rectus muscles could be faintly seen through the conjunctiva, as could their insertions, which ended in a perpendicular line close to the spots.

#### SUMMARY AND CONCLUSIONS

A review of the literature concerning the clinical entity which I term "senile hyaline scleral plaques" is presented. In addition to the cases reviewed from the literature, I report 5 cases of my own.

It is my belief that this interesting condition of the sclera would be found more frequently if ophthalmologists were on the alert for such a defect during their routine clinical examinations. Patients are frequently not aware of the presence of the plaques.

The terms "bilateral mesial superficial 'deficiency' of the sclera (scleral plaques)" (Graves<sup>11</sup>), "scleral plaques" (Culler<sup>12</sup>) and "hyaline scleral plaques" (Boshoff<sup>22</sup>) all fail to indicate one important feature of the disease. Since advanced age is probably the most important predisposing factor in the disease, it is my opinion that the term "senile hyaline scleral plaques" describes the disease more completely and accurately.

58 East Washington Street



# TRAUMATIC IRIDODIALYSIS ITS SURGICAL CORRECTION

## REPORT OF A CASE

AARON BARLOW, M D, AND HERMAN L WEINER, M D

PHILADELPHIA

A direct blow on the eye will sometimes cause a detachment of the root of the iris from its ciliary insertion—traumatic iridodialysis. When the separation is small, it is of no concern either from a visual or a cosmetic viewpoint. Frequent instillations of atropine and protection from light by dark glasses or a bandage may result in a reattachment, according to some authors. However, when the separation is large, it may cause monocular diplopia, owing to a double pupil. But of even graver concern in some cases is the unsightly cosmetic effect produced by the distortion of the normal contour of the iris and pupil. When the victim of the accident is a little girl, as in the following case, one has a strong desire to do something to correct the deformity.

### REPORT OF CASE

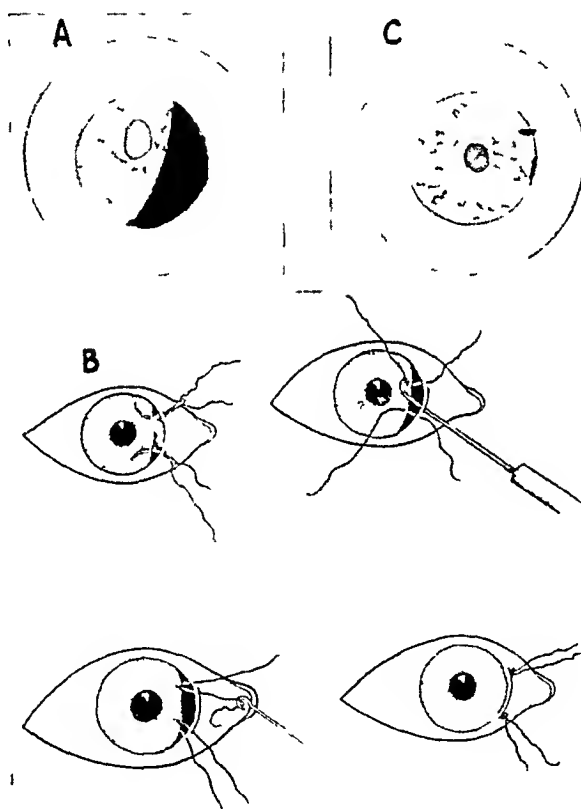
A girl aged 6 was struck in the left eye with a BB shot while playing in the street. She was admitted to the Mount Sinai Hospital on April 28, 1943, soon after the accident. The eye was intensely injected, and the anterior chamber was filled with blood. The temporal base of the iris, from 1 to 6 o'clock, was torn away from its ciliary attachment, forming a large separation, about 5 mm wide in the horizontal meridian. The pupil was distorted and drawn nasally and upward. The fundus could not be seen because of the hemorrhage in the anterior chamber. In treatment atropine, an antiseptic collyrium and sterile dressings were used. As the hyphemia gradually cleared, a fairly good view of the fundus could be obtained through the pupil, but not through the dialysis. Apparently, the rupture caused a separation of the stroma of the iris from its underlying pigment layer. The pigment layer thus prevented a view of the fundus through the dialysis. Later the lens also became opaque, forming a traumatic cataract (fig A).

The following ingenious operation, with its gratifying result, was devised by Jameson and has been described by Wiener and Alvis.<sup>1</sup> Jameson's original article, with a report of 4 cases, was published in 1909 in the *ARCHIVES OF OPHTHALMOLOGY*.<sup>2</sup> The technique, which we closely adhered to, is as follows:

A small, curved eye needle, threaded with fine silk (we used 000000), is introduced in the sclera 2 or 3

mm behind the limbus above the horizontal line, passed into the anterior chamber, transfixing the base of the torn iris, and passed out through the cornea. The needle is then removed. A similar suture is then passed below the horizontal line. An incision is then made in the limbus with a narrow keratome between the points of entrance of the two needles in the sclera. Through this opening a small, blunt iris hook is introduced, the hook engages that part of the thread between the iris and the cornea, pulling the end of the thread out of the cornea, back into the anterior cham-

ber and through the wound out of the eye. The threads are then tied, gently bringing the torn base of the iris back to the sclerocorneal junction (fig B). This operation was performed on Oct 10, 1943, about six months after the injury. Atropine was instilled and the eye bandaged. The postoperative course was uneventful. The eye was redressed on the second day and atropine instilled daily thereafter. The sutures were removed on the eighth day, and the child was discharged two days later. Subsequently (about three



A, diagram showing appearance of the eye before operation, B, drawing from Jameson,<sup>2</sup> illustrating technique of operation, and C, diagram showing appearance after operation.

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Read before the Section on Ophthalmology of the College of Physicians, Philadelphia, March 15, 1945.

1 Wiener, M, and Alvis, B Y. *Surgery of the Eye*, Philadelphia, W B Saunders Company, 1939.

2 Jameson, P C. Reattachment in Iridodialysis. A Method Which Does Not Incarcerate the Iris, *Arch. Ophth.* 38 391, 1909.

months later), on Jan 13, 1944, the traumatic cataract was removed by a discission and, again, on June 29, by a capsulotomy. The result was a clear, fairly round pupil (fig C). A small, very fine chink between the points of entrance of the two needles is visible on close inspection. The corneal needle punctures were invisible after several months but are distinguishable with the slit lamp. An approximate correction with a 12 D lens gave 20/70 vision. When the child is older and more cooperative, a careful refraction will probably give better results, since the fundus appears to have escaped serious damage. Vision in the right eye was 20/20.

## COMMENT

Reports in the literature on the surgical treatment of traumatic iridodialysis are not numerous. Most of the operators have used the method of incarceration of the iris, either by pulling the base of the iris into the limbal incision or by suturing with one or more sutures a few of the iris fibers to the scleral junction immediately behind the cornea. Bulson<sup>3</sup> reported 3 cases in which the method of incarceration of the iris was used, and Goldfeder<sup>4</sup> reported 2 cases in which the same method was employed, with successful results. Key<sup>5</sup> reported 4 cases in which operation was successfully performed by the suture method. Spaeth<sup>6</sup> describes a similar operation, also based on the principle of incarceration of the iris, which he prefers to do under a conjunctival flap in order to prevent infection from the exposed sutures. However, if the operation is done under aseptic conditions and with a sterile culture, the danger of infection should be no greater than in any other intraocular operation in which sutures are used—cataract extraction, for example. Wheeler<sup>7</sup> looked with disfavor on the method of incarceration of the iris, which, he said, "drags the iris into the limbus wound in such a way as to form an iris prolapse." Neither did he approve of sutures, on the general ground that "sutures should not be passed through eye structures unnecessarily." He maintained that "an attachment can be easily and permanently secured by simply carrying a tiny shred of tissue from the torn edge of the iris very slightly into the limbus wound."

3 Bulson, A. E., Jr. Correction of Iridodialysis by Operation, *Am J Ophth* 3: 357, 1920.

4 Goldfeder, A. E. Ueber die operative Behandlung der Iridodialyse, *Klin Monatsbl f Augenh* 89: 229, 1932.

5 Key, B. W. Iridodialysis as a Clinical Entity, *Am J Ophth* 17: 301, 1934.

6 Spaeth, E. B. Principles and Practice of Ophthalmic Surgery, ed 3, Philadelphia, Lea & Febiger, 1944.

7 Wheeler, J. M. Principles of Modern Surgery in Ophthalmology, *Am J Ophth* 17: 683, 1934.

The Jameson operation does not incarcerate the iris between the lips of the wound but brings the torn surface in contact with a freshened surface, within the anterior chamber. Reattachment takes place by agglutination through a plastic exudate thrown out from the iris at the point of contact.

We have had no previous experience with the surgical treatment of traumatic iridodialysis, and we do not presume to judge the merits of this or of other methods. In this particular case we were fortunate to obtain the desired result with the method described, and of course we are pleased. At the time of writing, about a year and a half after the operation, there are no signs or symptoms of any late complications, and the iris is still intact. The right eye has remained normal throughout.

In conclusion, we wish to state that we are keenly conscious of the fact that this operation, like any other intraocular procedure, is not without its potential risks and should not be undertaken too lightly. One of the possible dangers is injury of the lens (when the lens is clear) during the operation, thus producing a traumatic cataract. Secondary glaucoma as a possible late complication is mentioned by some authors. However, as far as we know, no case of secondary glaucoma following the surgical correction of traumatic iridodialysis has ever been reported. The operation should not be performed when the dialysis is small or when the defect is concealed by the lids. However, when the defect is large and the cosmetic effect is such that it can be a source of real embarrassment, the operation, we believe, is justified.

## SUMMARY

A case of extensive traumatic iridodialysis in a 6 year old girl, successfully corrected by the Jameson operation, is reported.

The technic of the operation, with illustrative drawings, is described in detail.

The child has been under observation for about a year and a half since the operation, and during all that time there have been no signs or symptoms of any late complications.

## DISCUSSION

DR WARREN S. REESE, Philadelphia. It might be possible to avoid a keratome incision by using a self-threading needle and two sutures, one of which is passed between the two strands of the first suture just beyond its exit from the iris. The needles could be removed after perforation of the cornea. The suture could

then be pulled back into the anterior chamber, one acting as a plug and preventing the other from slipping back through the iris

DR JAMES S SHIPMAN, Philadelphia In reading the technic of this operation, I could not understand why the cornea would not be badly scarred in cases of iridodialysis sufficiently large to justify this operation

Certainly infection is also a danger, since the needles and sutures pass out through the cornea,

and the free suture has again to be pulled back into the anterior chamber My experience with suturing the cornea has been that one is more likely to get sloughing, with infection about the sutures, than when suturing the sclera

I do not feel that the conjunctival flap is necessary On the other hand, one is probably better off without a conjunctival flap, which is likely to dam up the secretions and give rise to more slough about the sutures

# TESTS FOR DETECTION AND ANALYSIS OF COLOR BLINDNESS

## I AN EVALUATION OF THE ISHIHARA TEST

LE GRAND H HARDY, M D , GERTRUDE RAND P H D ,

AND

M CATHERINE RITTLER, B A

NEW YORK

Because of their great convenience and apparent simplicity of administration, polychromatic charts for the detection of defective color vision have been widely used in military and industrial fields for many years. Much dissatisfaction has been reported, and both the statistics of the Civil Aeronautics Administration and the results obtained by the Color Blindness Committee (Army Air Forces, United States Navy, Civil Aeronautics Administration and Inter-Society Color Council) indicate that, as they are used at present, polychromatic test plates are only about 50 per cent effective in screening out persons with defective color vision by the criterion of the test itself.

In an endeavor to discover the reason for this failure, extensive investigations have been undertaken at the Knapp Memorial Laboratories utilizing a large battery of tests on all types of subjects, ranging from persons with normal to those with extremely defective color vision. Our results indicate that while defects in the tests themselves account for part of the discrepancies, other important sources of error have arisen, namely (1) disregard of the critical importance of illumination, (2) careless and inefficient administration, (3) incompetent and invalid interpretation of results, (4) misapplication of the test to fields for which they were not intended, or the expectation of more from the tests than they were capable of or designed for, yielding

One of us (L H H) has for years insisted on the critical importance of the illumination used for viewing materials seen by reflected light, claiming that as they are at present administered polychromatic tests have become as much tests of the lighting system used as they are tests of the subject's color discriminatory ability.

Likewise, he has asserted that results obtained from polychromatic test plates, with their low values and chromas and large patterns yielding

dim and extensive retinal images, must with great caution be applied to situations requiring the recognition of luminous objects which yield small but bright retinal images. In the absence of time and facilities for carrying out complete colorimetric investigations, at least two types of tests should be given a subject before a complete diagnosis is made: one type using reflected light (polychromatic plates, matching chips, 100-hue test or dichotomy test), the other using luminous signals (anomaloscope, spectroscope, lantern or threshold test).

This report summarizes a critical evaluation of the Ishihara test plates taken as a representative type of polychromatic plates used for the detection and classification of observers with defective color vision. (The effect of quality of illumination on the results will be reported separately.) With minor changes, this evaluation can be applied to other plates of the same type (Stilling's, Rabkin's and the recent American Optical Company's issue of selected plates for the use of the armed services). All have particular merits and defects, and even in different editions of the same test there are to be noted marked, and sometimes critical, variations due to changes in printing inks, printing papers, printing processes and age. The use of linseed oil bases for inks is hardly conducive to permanence of printed colors.

"Pseudo-isochromatic" means apparently or falsely equal colors, that is, the colors are trickily chosen to fall within the color diagram zones where the defective observers are most likely to be trapped. Since the apparent color of any object can be changed by modifying the light used to view it, all these plates must be viewed under special external conditions. The Ishihara plates are not particularly critical, and this is one of their defects. Such plates can be made very critical, but in so doing the effect of the illuminant is enhanced.

The Ishihara Test for Colour-Blindness was devised by Dr Shmoubu Ishihara, professor of ophthalmology, medical department, Imperial

From the Knapp Memorial Laboratories, Institute of Ophthalmology

University of Tokyo, and was first described by him in 1917, when he was instructor at the military Medical Academy in Tokyo.<sup>1</sup> Since that time the test has run through eight or more Japanese editions, in the course of which some changes have been made in the colors used and in the number of plates in the series, although the basic principles have remained unaltered. The first edition (1917) we have been able to inspect through the courtesy of Dr Arnold Knapp, professor emeritus of ophthalmology, Columbia University College of Physicians and Surgeons, New York, who has in his library a complimentary copy of this little known edition. In this edition the introduction is less complete than in the later editions, the red-purple pigment is bluer than was used later, and plates 8 and 9 consist of an entirely different color combination. These plates as first published showed the digits composed of small blue-green disks on a background of small yellow and violet disks. In all later editions the digits are composed of green disks and the background of yellow and red-purple disks. The second edition was copyrighted in 1920,<sup>2</sup> and later editions, through the sixth, are close copies of this. A third edition was published in 1922 and a fourth in 1924. These were distributed in this country by E. B. Meyrowitz, Inc., of New York. The first publication on the use of the Ishihara test in this country was in 1924, by Clark,<sup>3</sup> who gave us the information that the original plates were destroyed in the Japanese earthquake of 1923. A fifth edition appeared in 1925, at which time C. H. Stoelting Co., of Chicago, was made the sole distributing agent in the United States, and a sixth edition in 1932. These two editions became widely known and used in this country. Like the earlier editions, they consist of 16 plates: the first plate for demonstration and the detection of color malingering; the 12 succeeding plates for the detection of congenital color blindness of the red-green type and of monochromasy in literates and the last 3 plates for the detection of this defect in illiterates. A seventh edition appeared in 1936, an eighth in 1939 and a ninth in 1940.<sup>4</sup> These three

editions contain 32 plates, the original 16 and 16 new plates of the same type but carrying different patterns. There are also some change in the pigments and a more liberal use of the two digit plate. The ninth edition was reprinted in London in 1943.

The fifth, seventh and ninth (British reprint) were the only editions available to us for experimental work and were, therefore, the ones used in the present study, and in a study to be reported separately, for a comparison of their value in detecting and analyzing deficiency in color vision.

In the words of the author of the test series

this series of plates is intended to discover quickly and accurately congenital colour-blindness, the most common form of colour-blindness. Congenital colour-blindness is of two kinds, total colour-blindness and red-green blindness, and these have each two forms, complete and incomplete. Incomplete total colour-blindness is the result of deficiency in the red-green sense and an accompanying weakness of the blue-yellow sense.<sup>5</sup>

Ishihara further classifies red-green blindness into red blindness (the type called by von Kries protanopia) and green blindness (called by von Kries<sup>6</sup> deuteranopia). Ishihara designates red blindness and green blindness also as complete and incomplete but does not describe what he means by this designation. He makes no claim to detecting the degree or extent of the color defect, i. e., a qualitative but not a quantitative evaluation is indicated. However, no critical score is given to indicate the dividing line between poor but normal color vision and defective color vision.

In constructing his test plates, Ishihara was obviously influenced by Stilling's Pseudo-Ischromatic Plates for Testing the Color Sense, but no plates are a direct copy and certain innovations are made.

The plates intended for testing color-blind literates consist of six series, 2 plates of each series in the fifth edition and 4 of each series in the seventh and ninth editions.

In series 1, which might be called a "transformation pattern" series, a digit composed in general of blue-red and yellow-red disks, varying from 1 to 5 mm in diameter, is seen by the subject with normal color vision on a background composed of yellow-green and blue-green disks of these sizes, the disks of both digit and background varying as to chroma and value. For the subject with defective red-green vision, the yellow-green

1 Ishihara, S. Tests for Colour-Blindness, Hanyu, Tokyo, Hongo Harukicho, 1917.

2 Dr Janet Howell Clark, professor of biophysics and dean of women of the University of Rochester, and Dr Anna M. Baetjer, associate in physiological hygiene, School of Hygiene and Public Health, Johns Hopkins University, gave us access to this edition. The book is a complimentary copy belonging to the late Dr W. H. Howell, former professor of physiology and director of the School of Hygiene and Public Health, Johns Hopkins University.

3 Clark, J. H. The Ishihara Test for Color Blindness. *Am J Physiol Optics* 5:269-276 (July) 1924.

4 Mr R. Koller, of C. H. Stoelting Co., Chicago, gave us access to the sixth, eighth and ninth (Japanese) editions.

5 Ishihara, S. ed 5, Tokyo, Kanehara, 1925.

6 von Kries, J. Ueber Farbensysteme, *Ztschr f Psychol u Physiol d Sinnesorgane* 13:241-324, 1897.

disks of the background and the yellow-red disks of the digit are indistinguishable, and a pattern is formed of the blue-red and blue-green disks which appear to him as a bluish digit on a yellowish background. The pattern is thus transformed for the subject with defective color vision into a different digit from that seen by the subject with normal color vision, e g, from an 8 to a 3. This series, as presented in the fifth edition, traps deuteranopes only.

Series 2 also is a transformation series, but with the colors of background and pattern reversed, that is, blue-green and yellow-green disks form the digit on a background of yellow-red and blue-red disks. As in series 1, the subject with defective color vision sees a bluish digit on a yellowish background. All subjects with defective color vision fail this series when tested with the fifth and seventh editions.

Series 3 and 4 are of the "vanishing digit" type, used by Stilling. In series 3 the digit is formed of yellow-red disks on a background of yellow-green and blue, and in series 4, of blue-green disks on a background of blue-red and yellow. These digits are plain to subjects with normal color vision but are rarely seen by subjects with defective color vision unless the defect is slight. This series fails to trap many deuteranomalous subjects and observers with low color discrimination.

Series 5 contains a "hidden digit," which supposedly is seen only by persons with defective color vision but is too often quite visible to subjects with normal color vision as well. The series has little diagnostic value.

Series 6 consists of two digits (e g, 26), one in red and one in red-purple disks on a background of gray disks of different brightness. Protanopes, whose neutral region is in the red, are supposed to see only the red-purple digit (the 6), and deuteranopes, whose neutral region is in the red-purple, only the red digit (the 2). This series helps to differentiate dichromasy from trichromasy and is adequate to classify only deuteranopes as to type of defect.

The remaining plates are for testing illiterates, who are instructed to follow "with their eye" a winding line between two terminal x's. In some of the plates this is an easy task for subjects with normal color vision but is difficult for subjects with defective color vision, in others the path is readily visible to subjects with defective color vision but is not plain to persons with normal color vision. These plates are difficult to administer and score, and since only literates were included among the subjects used in the present study, they will not be considered further.

#### EVALUATION OF THE FIFTH EDITION OF THE ISHIHARA TEST AS A MEANS OF DETECTING AND CLASSIFYING DEFECTIVE COLOR VISION

The Ishihara test (fifth edition) was included as one test in a battery used in the Knapp Memorial Laboratories to study the persons with defective color vision referred to the laboratories. These subjects were not selected on the basis of any statistical survey. They included patients referred to us by ophthalmologists, men who had been rejected by the armed forces on the basis of defect in color vision and subjects obtained from some of the New York city high schools, from the Vanderbilt Clinic and from other sources. The battery included the following tests, which have been described in the literature.

Ishihara Tests for Colour-Blindness (fifth edition) <sup>5</sup>

Rabkin Polychromatic Plates for Testing Colour Vision (second edition) <sup>7</sup>

Pseudo-Isochromatic Plates for Testing Color Perception, engraved and printed by Beck Engraving Co, Inc, and published and distributed by the American Optical Company <sup>8</sup>

Farnsworth-Munsell 100-Hue Test <sup>9</sup>

Farnsworth Dichotomous Test <sup>9</sup>

Inter-Society Color Council Single Judgment Test for Red-Green Discrimination <sup>10</sup>

Nagel's anomaloscope <sup>11</sup>

Several additional tests were used which have not as yet been described in print, notably a series of polychromatic plates and a new form of anomaloscope devised in this laboratory. The results of the entire battery of tests aided in the classification of the type and extent of the defects in color vision. Our data thus permit us to evaluate each of the aforementioned tests as a diagnostic or screening medium and as a medium for the differential classification of the type and extent of the defect <sup>12</sup>. The present

7 Rabkin, E. Polychromatic Plates for Testing Colour Vision, ed 2, Kharkov, State Medical Publishing House of the USSR, 1939.

8 American Optical Company. Pseudo-Isochromatic Plates for Testing Color Perception, Philadelphia and New York, Beck Engraving Co, 1940.

9 Farnsworth, D. Farnsworth-Munsell 100-Hue and Dichotomous Tests, J Optic Soc America **33**:568-578 (Oct) 1943.

10 Hardy, L. H. Single Judgment Test for Red-Green Discrimination, J Optic Soc America **33**:512-514 (Sept) 1943.

11 Nagel, W. A. Zwei Apparate für die augenärztliche Funktionsprüfung. Adaptometer und kleines Spektralphotometer (Anomaloskop), Ztschr f Augen **17**:201-222, 1907.

12 A test for color blindness may be a simple diagnostic or screening medium in which case the purpose



paper, however, will be confined to the work with the Ishihara test, mention being made of the battery of tests because of its use in the classification of the subjects as to type and extent of defect. Because this battery of tests was so comprehensive, it is understandable why we chose for inclusion the fifth edition of the Ishihara test, consisting of 16 plates, rather than one of the longer editions. The comparison of results given by the various editions at our disposal was made on a smaller group of subjects, including some with each type of defective color vision. This work is reported separately.

The entire battery of tests was given to 106 subjects: 23 deuteranomalous and 12 protanomalous subjects (anomalous trichromats), 15 deuteranopes and 17 protanopes (dichromats), 7 persons showing generally low color discrimination sufficient to amount to a defect in color vision, and 32 persons who showed low color discrimination to a lesser degree which would not be sufficient to amount, in all probability, to a real defect in color vision. This last group we have classified as "low normal." This classification of subjects follows the scheme outlined by

is merely to screen out the subjects with defective color vision from those with normal color vision, or it may be a differential classifying medium, in which case it is designed to determine both the type and the extent of the defect. It is our belief that the ideal tests for color blindness should serve both functions. 1 For some purposes the simple screening test is adequate, and its simplicity of operation and interpretation is an advantage. 2 For such purposes as industrial employment, vocational guidance and other means of adapting the environment of the person with defective color vision so that it may best serve his practical and esthetic needs, it is important to know how much defect is present and how color stimuli appear to him. There are many vocations, such as automotive wiring, which are open to anomalous trichromats but which cannot be handled by dichromats. Even in this field distinctions must be made. For example, the anomalous trichromat who can distinguish the difference in color between new-coded wires viewed under good illumination is able to work on new motors, but he cannot distinguish this difference under flashlight illumination or when the wires have become soiled by use and is, therefore, unable to do repair work on the motors. It is often necessary, also, to know the type of defect and whether or not there is distortion of the brightness value of color stimuli. It would seem that a deuteranope, who has little, if any, distortion of the brightness aspect of the colors, would be useful in certain types of heterochromatic photometry, while the protanope, who sees the long wave end of the spectrum as darker and the short wave end as lighter than normal, could not do this work. Again, a deuteranope is less likely to distinguish between the customary red, green and amber traffic signals than the protanope, who sees the green signal as bright and the red one as dim. On the other hand, the protanope may find it difficult to see a red traffic signal during night driving.

two of us (L. H. H. and G. R.)<sup>13</sup> For the classifying of anomalous trichromasy particular reliance had to be placed on the results with the anomaloscope, our special polychromatic plates and the Farnsworth Dichotomous Test, for the classifying of low color discrimination and low normal color vision on these tests and, in addition, on the Farnsworth-Munsell 100-Hue Test.<sup>14</sup>

For all work with pigment test material a close approximation to I C I Illuminant C was used (Illuminant C approximates a color tem-

13 Hardy, L. H., and Rand, G. Recent Developments in Color Vision Testing, Graduate Lecture, American Academy of Ophthalmology Outlines of Instructional Courses, Continuous Course No. 6 and 7, 1944. Hardy, L. H., Rand, G., and Rittler, M. C. Color Vision and Recent Developments in Color Vision Testing, Arch. Ophth., to be published.

14 To persons not familiar with the classic terminology of color blindness and those to whom our article<sup>13</sup> is not available, the following simple explanation of terms may be of value.

In the Young-Helmholtz theory there are three factors in the color vision process: (1) the red primary, proto, or first, process, (2) the green primary, deuto, or second, process, and (3) the blue primary, trito, or third, process. Hence one would expect to find three types of color vision: (1) trichromatic, in which all three processes function, (2) dichromatic, in which only two processes function, and (3) monochromatic, in which there is only one differentiated physiologic process. Trichromatic color vision means that all three processes are functioning, but since one or more of the processes may function aberrantly, there will be as a result three types of trichromatic color vision: (1) normal, (2) anomalous, in which one or more of the processes is weak, and (3) low discrimination, in which apparently all processes are weak. Anomalous trichromasy is designated according to the process which is weak as (1) protanomaly, or predominantly red weak, (2) deuteranomaly, or predominantly green weak, and (3) tritanomaly, or predominantly blue-yellow weak. Dichromatic color vision means that only two of the processes are functioning and hence is similarly divided into three types: (1) protanopia, formerly called red blindness, (2) deuteranopia, formerly called green blindness, and (3) tritanopia, formerly called blue-yellow blindness. As a mnemonic, we might point out the recurrent triad. There are three kinds of abnormal color vision: (1) anomalous trichromasy (three types—protanomaly, deuteranomaly and tritanomaly), (2) dichromasy (also three types—protanopia, deuteranopia and tritanopia), and (3) monochromasy. Protanopia exhibits a shortened red end of the spectrum, a neutral area at about 493 millimicrons (in the blue-green), a second neutral band in the red (at 493 c) and a brightness peak, which is shifted toward the violet. Deuteranopia shows a neutral region in the green (at about 497 millimicrons), a second neutral band in the red-purple (at 497 c) and no shift in the luminosity peak. Tritanopia shows a shortened blue end of the spectrum and a neutral band in the yellow-green. The luminosity peak is not shifted. These types, as well as corresponding anomalous trichromatic types, are best detected and classified by anomaloscopic tests.

perature of 6750° K and represents average overcast skylight or average daylight ) This was obtained from the combination of a 100 watt gas-filled tungsten filament lamp (color temperature 2848° K ) and a Macbeth daylight glass filter, the combination giving a color temperature of 6700° K <sup>15</sup>

The illumination on the test material was about 25 foot candles The testing distance in the case of polychromatic test plates was about 30 inches (76 cm ) Responses should be immediate (within two seconds) Hesitant or studied responses are viewed with suspicion

The results for the Ishihara test, fifth edition, are summarized in tables 1 to 4 They will be discussed under three headings (1) analysis of the individual plates, (2) significance of performance score on the entire test, (3) differential classification of deuteranopia and protanopia, deuteranomaly and protanomaly

for the subjects with defective color vision as a group and for the subjects with low normal color vision as a group This comparison shows the value of each plate as a diagnostic or screening medium

In this table it is seen that the plates of series 2 are the only ones which were failed by all the subjects with defective color vision Plate 4 of this series was passed by all the subjects with normal color vision, and plate 5 by only 78 per cent of this group Plate 4 is therefore unique in that all the subjects with defective color vision fail it and all the subjects with normal color vision pass it Judged by our observers, then, this plate when properly administered furnishes an ideal screening or diagnostic test, used with Mazda light, as will be shown separately, its efficiency for detection of deuteranomalous subjects drops from 100 to 43 per cent The remaining plates are much less successful For

TABLE 1—*Analysis of Individual Plates in the Ishihara Test, Fifth Edition*

Type of Defective Color Vision	Number of Subjects	Percentage of Subjects with Each Type Passing Individual Plates											
		Series No											
		1		2		3		4		5		6	
		Plate No	Plate No	Plate No	Plate No	Plate No	Plate No	Plate No	Plate No	Plate No	Plate No	Plate No	Plate No
		2	3	4	5	6	7	8	9	10	11	12	13
Anomalous Trichromasy													
Deuteranomaly	23	43	43	0	0	13	22	17	39	13	0	17	30
Protanomaly	12	67	67	0	0	0	0	8	8	0	0	8	17
Dichromasy													
Deuteranopia	15	0	7	0	0	0	0	0	0	0	0	0	0
Protanopia	17	53	59	0	0	0	0	0	0	24	18	0	0
Low discrimination	7	57	71	0	0	14	57	14	43	0	0	43	86
All types of defective color vision	74	42	46	0	0	5	12	8	18	9	4	11	20
Low normal color vision	32	100	100	100	78	87	100	100	94	87	84	97	97

*Analysis of the Individual Plates*—In table 1 is shown for the subjects with each type of defective color vision and for the subjects with low normal color vision the percentages who pass the individual Ishihara plates, designated by both series number and plate number The first five horizontal rows of figures show these percentages for each type of defective color vision and demonstrate the value of the individual plates for detecting each type The lower two rows present for comparison the percentages

15 The Macbeth Daylighting Company has designed an excellent table lamp and book rest to provide convenient, standard conditions for tests of the polychromatic plate type The color temperature of the illumination supplied is 6800° K, the amount of illumination on the test material is about 40 foot candles, the illumination is even and falls on the test material at an angle of approximately 45 degrees, and the test material is supported so that it is viewed at an angle of 90 degrees The complete unit, which is called the Macbeth Easel Lamp, provides ideal lighting conditions for the administration of color tests of this type It is supplied by the Macbeth Daylighting Company, 227 West Seventeenth Street, New York

example, the plates of series 3 serve to detect deuteranopes, protanopes and protanomalous subjects but not all deuteranomalous subjects or observers with low color discrimination, the plates of series 4 and 6 detect deuteranopes and protanopes but not all deuteranomalous and protanomalous observers or subjects with low discrimination, the plates of series 5 detect deuteranopes and protanomalous subjects and observers with low discrimination but not all deuteranomalous subjects or protanopes The plates of series 1 are the least effective, except for deuteranopes They are particularly ineffective for protanopes and protanomalous subjects who tend to see the digit (which is composed of dominantly reddish disks) as a dark figure and the background (which is composed of greenish disks) as light For this reason more than 50 per cent of protanopes and 67 per cent of protanomalous subjects pass these plates Protanopes pass the plates of series 5, too, in a higher percentage than would be expected, that is, they fail to see the "hidden digit" It is because of their

success with the plates of series 1 and 5 that protanopes achieve, on the average, a higher performance score on the entire test than deuteranopes and nearly the same score as protanomalous subjects (table 2)

*Significance of Performance Scores on Entire Test*—Table 2 shows the performance scores obtained on the entire Ishihara test. In this table are given for each type of defective color vision and for low normal vision (a) the average score achieved by each group, (b) the median, or middle, score for each group and (c) the range

TABLE 2—Significance of Performance Score<sup>\*</sup>

Type of Defective Color Vision	No. of Subjects	Average Score	Median Score	Range of Scores
Anomalous Trichromasy				
Deuteranomaly	23	20	17	0-58
Protanomaly	12	15	17	0-33
Dichromasy				
Deuteranopia	15	1	0	0-8
Protanopia	17	13	17	0-33
Low discrimination	7	31	25	8-58
All types of defective color vision	74	15	13	0-58
Low normal color vision	32	94	100	75-100

\* The performance score is the percentage of the 12 plates to which correct responses were given.

of scores, from lowest to highest, achieved by the subjects within each group. A score of 100 indicates that correct responses were given to all 12 plates, a score of 0, that no correct responses were given, and scores between 0 and 100 indicate the percentage of the 12 plates to which correct responses were given. As in table 1, the first five horizontal rows of figures give the data for the subjects with each type of defective color vision and the lower two rows, the data for the subjects with defective color vision as a group and for the subjects with low normal color vision as a group.

In table 2 it is seen that (a) the subjects with defective color vision as a group have an average performance score of 15 and the subjects with low normal vision a score of 94, (b) deuteranomalous subjects have an average score of 20 and deuteranopes an average score of 1, and (c) protanomalous subjects have an average score of 17 and protanopes an average score of 15. On the average, then, on the basis of the performance scores, the Ishihara test would seem to separate persons with defective color vision from those with normal color vision and deuteranomalous subjects from deuteranopes. However, for the purpose of screening or of classification, it is not the average score achieved by a group that is important but the score achieved by the individual subject. This is shown in the last column of table 2, in which for each type of defective color vision is given

the range of scores, from lowest to highest, achieved by the subjects having that type of defect. This column shows clearly the overlapping of scores between the groups with the various types of defective color vision and thus demonstrates the impossibility of classifying the type of color defect on the basis of score alone. There is, however, no overlapping of scores between the group of subjects with defective color vision taken as a whole and the group of subjects with low normal color vision, the lowest score of the latter group being 75 and the highest score of the former being 58. In round numbers, then, it would seem that a critical score of 60 might be accepted as the dividing line between the performance of subjects with defective color vision and normal performance on the Ishihara test.

The overlapping of scores between groups with the various types of defective color vision is brought out still more clearly in table 3, which shows the distribution of performance scores for each type. For representation in this table, the following classification of performance scores was made: 0 (failure on all plates), 8 to 17 (passing 1 or 2 plates), 25 to 42 (passing 3 to

TABLE 3—Distribution of Performance Scores on the Ishihara Test (Fifth Edition)

Type of Defective Color Vision	No of Sub jects	Number of Plates Passed						
		0	12	35	68	911	12	
		Percentage of Each Group Achieving Scores of						
		0	8 17	25 42	50 67	75 92	100	
Anomalous Trichromasy								
Deuteranomaly	23	30	35	22	13	0	0	
Protanomaly	12	25	50	25	0	0	0	
Dichromasy								
Deuteranopia	15	93	7	0	0	0	0	
Protanopia	17	18	76	6	0	0	0	
Low discrimination	7	0	29	43	29	0	0	
All types of defective color vision	74	36	41	14	9	0	0	
Low normal color vision *	32	0	0	0	0	47	53	

\* In this group, 53 per cent passed all 12 plates (score 100), 22 per cent passed 11 plates (score 92), 22 per cent passed 10 plates (score 83), and 3 per cent passed 9 plates (score 75).

5 plates), 50 to 67 (passing 6 to 8 plates), 75 to 92 (passing 9 to 11 plates), and 100 (passing all plates). The overlapping of scores between the groups with the various types of defective color vision is clearly shown in this table, and consequently the inability of the Ishihara test to yield a classification of either type or extent of defect on the basis of performance score.

The following points are brought out in tables 2 and 3:

1. The scores of deuteranomalous and protanomalous subjects and of observers with low

color discrimination have a wider range of scatter than those of deuteranopes and protanopes. That is, as seems probable, their defect may vary from a slight to an extreme anomaly of low discrimination, while dichromats having a defect in red-green vision would present a more homogeneous group, at least when studied by means of tests designed primarily to detect defects in red-green vision.

2 All persons with defective color vision of the red-green types, as well as persons having low color discrimination amounting to a defect, are screened from the group having normal and low normal color vision if 60 is taken as the critical score on the Ishihara test (fifth edition). In the group tested no subject with defective color vision achieved a score of more than 58, and no subject with low normal color vision had a score of less than 75.

adequate to separate subjects with defective color vision from those with normal color vision when the test is properly administered, but it is not adequate to make the equally important differential classification of type and extent of defect. It remains to discuss the type of response to certain plates as a clue to this classification.

In the Ishihara test the plates of series 6 are the only ones designed for this purpose. On these plates a double digit is presented (26 on plate 12 and 42 on plate 13). On each plate the left hand digit is composed of red disks, the right hand digit of red-purple disks and the background of gray disks. According to Ishihara, the subject with deuteranopic type of red-green blindness will be able to read only the red digit, and the protanopic type, only the red-purple digit. Our data have been analyzed to determine the effectiveness of these plates for making this differential classification.

TABLE 4—Analysis of Value of Plates 12 and 13 (Series 6) as a Means of Differentiating Deuteranopia and Protanopia, and Deuteranomaly and Protanomaly

Type of Defective Color Vision	Number of Subjects	Percentage of Subjects Correctly Classified by				Percentage of Subjects Incorrectly Classified by				Percentage of Subjects Not Classified by			
		Plate		Both Plates	Either Plate	Plate		Both Plates	Either Plate	Plate		Both Plates	Either Plate
		12	13			12	13			12	13		
Anomalous Trichromasy													
Deuteranomaly	23	65	65	57	74	0	0	0	0	35	35	43	26
Protanomaly	12	50	83	50	83	8	0	0	8	42	17	50	8
Dichromasy													
Deuteranopia	15	93	93	87	100	0	0	0	0	7	7	13	0
Protanopia	17	41	59	29	71	6	6	6	6	53	35	65	23

3 No cleancut separation as to extent or type of defect can be based on performance scores. While in general the dichromats had lower scores than the anomalous trichromats, a majority of the latter group (65 per cent of deuteranomalous and 75 per cent of protanomalous subjects) had scores between 0 and 17, the range which includes 100 per cent of the deuteranopes and 94 per cent of the protanopes tested. Scores cannot, therefore, be used to indicate either the extent or the type of the defect.

4 Of the deuteranopes tested, 93 per cent failed all the plates in the Ishihara test, of the protanopes, only 18 per cent failed them all. The fifth edition of this test, then, "traps" deuteranopes more decisively than persons with the other types of defective red-green vision.

*Differential Classification of Deuteranopia and Protanopia, and Deuteranomaly and Protanomaly*—So far we have discussed performance scores on the Ishihara test both as a means of detecting the presence of a defect in color vision and as a means of classifying the type of defect, and we have shown that the score achieved is

Difficulty is encountered when other types of response are given, such as the correct reading of both digits or of neither (in which cases, of course, no interpretation is possible) or the incorrect reading of one or both digits. In scoring the responses to these plates, the following plan was adopted. A subject was called "classified" as to type of defect by the plate in question when one digit was read correctly and the other was not seen at all or was read incorrectly. When both digits were read correctly, when neither was read correctly or when one was read incorrectly and the other was not seen at all, the subject was called "not classified." In short, "a hit and a miss" are necessary in order to utilize this plate as a test for differential classification. The results obtained are shown in table 4.

The following points are brought out in table 4.

1 The plates of series 6 are better designed to classify deuteranopes as to type of defective red-green vision than deuteranomalous observers. The failure in case of the latter group is due either to an incorrect reading of the significant digit or to a correct response to both digits.

2 The plates of series 6 are better designed to classify protanomalous observers as to type of defective color vision than protanopes. The failure in the latter group is due either to an incorrect reading of the significant digit or to inability to see any digit.

3 Plates 12 and 13 give equally good results for the deuteranopic type, but plate 13 is better than plate 12 for distinguishing the protanopic type (83 and 59 per cent with plate 13, as compared with 50 and 41 per cent for plate 12).

4 One protanomalous observer and 1 protanope of our group would have been classified as deuteranopes by one or both plates of series 6, with Mazda light; this number would have been greatly increased. None of the deuteranopic type were wrongly classified.

5 It is seen, for example, that whereas 41 per cent of the protanopes were correctly typed ("a hit and a miss") by plate 12, 59 per cent of this group were correctly typed ("a hit and a miss") by plate 13. However, if the indicated response was required from each plate (i.e., "a hit and a miss" on each plate), only 29 per cent of the protanopes were correctly typed. On the other hand, if the indicated response was required from only one of the two plates, and the results obtained from the other ignored, then 71 per cent of the protanopes were correctly typed, the second plate yielding an ambiguous response.

#### CONCLUSIONS

The following conclusions concerning the fifth edition of the Ishihara test seem justified:

1 Properly administered, the test affords a good rough device for screening persons with defective red-green vision from persons with normal color vision if a performance score of 60 is taken as the critical score. In the group tested, no subject with defective color vision scored more than 58 and no subject with low normal color vision less than 75.

2 No analysis as to type or extent of defect can be based on performance scores.

3 The test yields a lower score for the deuteranopic than for the protanopic type of defective color vision. (This is, in effect, a "weighting," which is lost with more yellowish illumination.)

4 The plates of series 6, which were designed to distinguish between deuteranopes and protanopes, are adequate to classify deuteranopes alone, when the report on either of the two plates is taken as indicative. On this basis, only 74 per cent of the deuteranomalous subjects, 83 per cent of the protanomalous observers and 71 per cent of the protanopes were correctly typed.

5 The Ishihara test is a gross test for defective red-green vision. It fails to classify the type of defective color vision (protanopia, protanomaly, deuteranopia, deuteranomaly, tritanopia, tritanomaly) and cannot be used to give a satisfactory evaluation of the extent or the degree of the defect, no matter how carefully administered.

6 Plate 4 is a practically perfect screening test when properly used, but if used with Mazda light, its efficiency drops from 100 to 43 per cent for deuteranomalous subjects.

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# STEREOSCOPIC SENSITIVITY IN THE SPACE EIKONOMETER

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Recent experimental work has shown that the space eikonometer is a suitable instrument for the measurement of aniseikonic errors<sup>1</sup> This instrument<sup>2</sup> differs from the standard eikonometer in that the measurement depends on binocular (stereoscopic) perception rather than on a direct comparison of image sizes In the space eikonometer all empiric clues which might affect the apparent relative positions of selected test elements are eliminated, and their apparent orientation can be perceived only by binocular (stereoscopic) space perception If an aniseikonic error exists between the two eyes, these test objects will appear incorrectly oriented to the subject according to the nature of the error present By means of suitable size lenses the relative sizes of the images in the two eyes can be changed until the test objects appear correctly oriented<sup>3</sup> The magnifications introduced to achieve this measure the aniseikonic error

To complete the study of the visual factors on which this instrument is based, the stereoscopic sensitivity for the particular test objects used under optimum conditions must be known The purpose of this paper is to report the results of a series of rather comprehensive experiments in which these sensitivities were determined

## DESCRIPTION OF INSTRUMENT

Only a brief description of the space eikonometer need be repeated here Complete descriptions and technics for operation can be found elsewhere<sup>4</sup>

From the Research Division of the Dartmouth Eye Institute, Dartmouth Medical School

1 Ogle, K N Association Between Aniseikonia and Anomalous Binocular Space Perception, *Arch Ophth* **30**:54-64 (July) 1943 Burian, H M, and Ogle, K N Meridional Aniseikonia at Oblique Axes, *ibid* **33** 293-310 (April) 1945 Ogle, K N, and Madigan, L F Astigmatism at Oblique Axes and Binocular Stereoscopic Spatial Localization, *ibid* **33** 116-127 (Feb) 1945

2 Ames, A, Jr The Space-Eikonometer Test for Aniseikonia, *Am J Ophth* **28** 248, 1945

3 Ogle, K N Theory of the Space Eikonometer, *Arch Ophth*, to be published

4 Ogle and associates<sup>1</sup> *Ames* <sup>2</sup>

As shown in figure 1, the apparatus consists of three parts (1) the arrangements for supporting and shielding the test elements, (2) a head support and (3) the optical test system

The test elements consist of an oblique cross and four plumb lines The cross is composed of two intersecting smooth red cotton cords stretched between the corners of a 5 foot (152 cm) square wooden frame, which is set up vertically a distance of 3 meters from the eyes of the subject The plane of the cross is set at right angles to and centered with respect to the objective median and horizontal planes of the subject A plumb line (smooth white cord) can be suspended through the center and in the plane of the cross

Two pairs of plumb lines (smooth cord) are set parallel to the plane of the cross, one pair (green) 60 cm to the front and the other (white) a similar distance

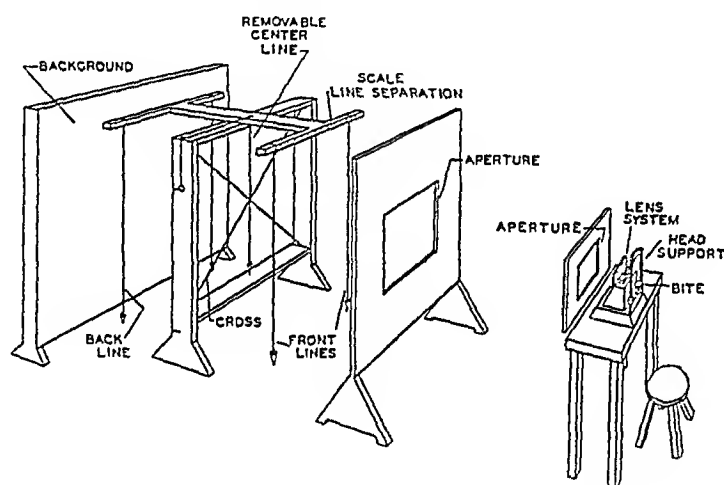


Fig 1—Perspective drawing of essential parts of apparatus for determining the sensitivity of the test elements of the space eikonometer

to the rear These cords are suspended from 2 meter sticks, which provide a means for locating the plumb cords at different separations

The test elements were seen against a background of stretched black velvet cloth In front of the elements, about 1 meter from the subject, was erected a screen (painted flat black), in which an aperture was cut This aperture restricted the field of view to the elements and prevented their ends from being seen The angular field of view was 21 degrees in the horizontal and 15 degrees in the vertical meridian

A uniform illumination was provided by four 18 inch (45.5 cm) (40 watt) Lumiline lamps arranged in a plane and equally spaced on each side of and above and below the center of the cross With this illumination the test elements appeared to stand out vividly against the black background, without shadows The brightness of the cords was about 0.6 millilamberts

The entire space between background and screen was enclosed by black sateen cloth The general illumination of the room, supplied indirectly by a 15 watt lamp, was low and diffuse



The head of the subject was held before the optical test system by forehead and temple rests and by a wax bite. This arrangement tends to eliminate head movements and depth perception clues from parallax.

To determine the stereoscopic sensitivity for the several test elements, the disparities between the images of these elements in the two eyes were modified and measured by an optical system before the eyes (fig 2). The optical system used in the experiments reported here consisted of an over all and a meridional adjustable size unit<sup>5</sup> before the left eye and the right eye, respectively. The meridional unit could be rotated so as to magnify only in the horizontal meridian (axis 90) or in the vertical meridian (axis 180). By means of an attachment to the meridional unit its magnification could be set and measured in steps of 0.05 per cent with a maximum error of 0.02 per cent<sup>6</sup>.

A device for changing the declinations between the images of the two eyes was mounted in front of the adjustable units. This consisted of two matched 2 per

## PROCEDURE AND METHOD

Three measurements are made on the space eikonometer which determine the aniseikonic error of a given subject. The image size difference in the horizontal meridian (axis 90) is determined by finding what magnification must be introduced before one eye in the horizontal meridian to cause the two front cords of the instrument to appear at the same distance from the subject. A method of limits is used. The image size difference in the vertical meridian (axis 180) is then determined by finding what magnification must be introduced before one eye in the vertical meridian in order to correct any apparent rotation of the cross about a vertical axis. The declination error<sup>3</sup> which is indicative of a meridional aniseikonic error at an oblique axis is determined by finding the angle through which the geared size lenses have to be turned to correct any apparent inclination of the cross about a horizontal axis. The purpose of this study is to obtain data on sensitivity for these three types of measurements.

The problem of determining the stereoscopic sensitivity of persons by finding a measure of the thresholds in such an experimental apparatus is primarily one of psychometrics. Several methods of determining these thresholds are generally recognized, but the so-called method of constant stimuli<sup>7</sup> is usually considered the most reliable. This method, as applied here, will be clear from the following discussion.

Consider the problem of finding a measure of the stereoscopic sensitivity (acuity) of a subject for the apparent displacements of the front vertical plumb lines of the space eikonometer. If one magnifies the image of the right eye by a given amount in the horizontal meridian, and thus changes the disparities between the retinal images of the two vertical lines in the two eyes, the right line will appear farther away from the subject than will the left line. If the size of the image is decreased in the horizontal meridian, the right cord will appear nearer than the left. The least change in magnification which will be recognized in an apparent displacement of the two cords would be a measure of the threshold and, therefore, of the sensitivity. Such a minimal change, however, will not always be recognized, and, again, sometimes even a smaller change will be seen, so that the problem becomes a statistical one. In what percentage of times will certain given changes in magnification be recognized in an apparent displacement of the two cords?

A few preliminary trials usually establish the approximate limits in change of magnification for which the right cord will first appear just farther away and then just nearer than the left cord. This range was then broken into five equally spaced changes in magnification, and each of these changes was presented to the subject 40 times in a random order<sup>8</sup>. Thus, a series of 200 judgments of random changes in magnification was obtained as to whether the right cord appeared farther or nearer than the left cord. So far as possible, the subject was asked to give either one or the other of

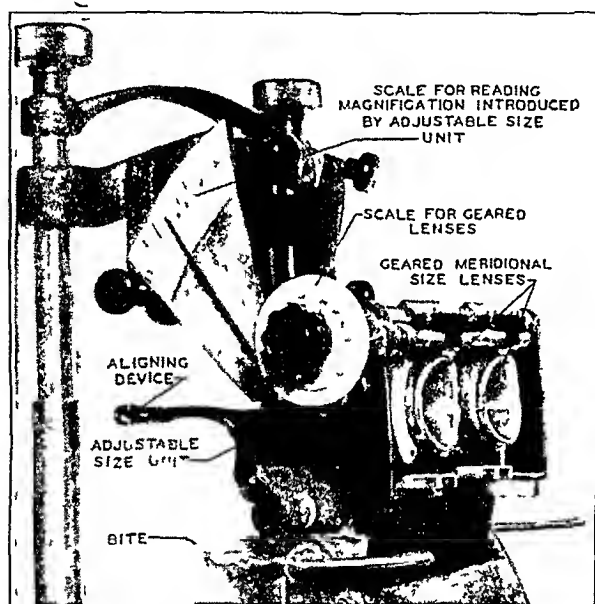


Fig 2—Photograph of the test lenses used in the study of the sensitivities of the space eikonometer

cent meridional size lenses mounted in geared rings and so arranged that they could be rotated equally but in opposite directions when activated by a screw. A drum with a scale was attached to the screw, to read the amount of rotation of the geared lenses. These lenses could be set, without significant error, in steps of 1.25 degrees, introducing a change in vertical declination of 0.05 degree.

Before the right eye a shutter was placed between the adjustable size unit and the geared lenses. When lowered, this occluded the right eye except for a small region (about 1 minute of arc) seen through a hole in the center of the shutter. This hole permitted binocular fixation of the center of the cross, when binocular perception of the test elements was interrupted, and kept the eyes properly converged.

5 Ogle, K. N. An Optical Unit for Obtaining Variable Magnification in Ophthalmic Use, *J Optic Soc America* 32:143-146 (March) 1942.

6 These values were determined on the so-called dioptrikonometer (Ogle, K. N., and Ames, A., Jr. *Ophthalmic Lens Testing Instrument*, *J Optic Soc America* 33:137-142 [March] 1943).

7 For a discussion of these methods see Guilford, J. P. *Psychometric Methods*, New York, McGraw-Hill Book Company, Inc., 1936, p. 166.

8 The random order was obtained from Fisher, R. A., and Yates, F. *Statistical Tables for Biological, Agricultural and Medical Research*, London, Oliver & Boyd, 1938, table 33, p. 82.

these responses, though occasionally a "can't tell" or a doubtful response was allowable<sup>9</sup>

The shutter was lowered immediately after a response from the subject, and all changes in the adjustable size unit were made while the right eye could see only the small central part of the cross

The tests were made under the same conditions as those observed when data are obtained with the space eikonometer. Consequently, no limit was placed on the time required by the subject to make a judgment, though on the average this varied between two and eight seconds. During this period the subject was also free to use ocular movements in making the judgment if he so desired. He was cautioned, however, to use the same criterion throughout a given experiment.

TABLE 1—Typical Set of Data Obtained for Determining a Measure of the Stereoscopic Sensitivity for the Front Cords on the Space Eikonometer<sup>2</sup>

Magnification Setting, Percentage	Judgment Category	Number of Judgments in Each Category	Percentages †
0.90	Nearer	2	5.1
	Doubtful	1	
	Farther	37	94.9
0.85	Nearer	10	26.3
	Doubtful	2	
	Farther	28	73.7
0.80	Nearer	24	64.9
	Doubtful	3	
	Farther	13	35.1
0.75	Nearer	31	79.5
	Doubtful	1	
	Farther	8	20.5
0.70	Nearer	39	97.5
	Doubtful		
	Farther	1	2.5

<sup>2</sup> The number of judgments in which the right cord appears either "nearer" or "farther" than the left cord is shown as the magnifying unit before the right eye is changed in five different steps. The separation of the cords was 50 cm, corresponding to a visual angle of 12 degrees.

<sup>†</sup> The doubtful judgments were divided among the other two categories in proportion to the number of judgments in the "nearer" and the "farther" category.

The experiment was divided into two parts, of 100 judgments each, with a rest period of five to ten minutes between the parts. In any given experiment if the judgments were found difficult to make one minute rest periods were permitted after each 25 judgments, to reduce the possible effect of fatigue.

#### TREATMENT OF DATA

The data obtained in any experiment consisted of the number, and therefore the percentage, of the judgments for each magnification setting in which the right cord was judged to be "nearer" or "farther" than the left cord. These data can be studied graphically, a typical set of which is given in table 1 and illustrated in figure 3. The type of curve that describes these data is the well known psychometric curve.

That magnification setting for which 50 per cent of the judgments were "farther" and 50 per cent "nearer" indicates the most probable relationship between the relative size of the images in the two eyes for which

9 Here, a three category experiment was used. The number of doubtful responses was small, and for each stimulus these were distributed in the "nearer" and the "farther" category in proportion to the number of judgments in those categories. This procedure is today considered the proper way to treat doubtful responses (Guilford<sup>8</sup>).

the two front cords appeared at the same distance. At this setting of the test lenses the judgments were made by pure guesswork, and the distribution found was due solely to chance. At the extremes of the curve, there is nearly 100 per cent certainty that the apparent displacements of the cords due to the change in magnification from the 50-50 per cent point would be seen. Between these limits the proportion of judgments varies from near certainty to pure chance. From this curve the threshold of stereoscopic sensitivity can be read off directly, the value depending on what percentage of certainty one chooses to consider as the threshold point.

The entire psychometric curve for a given set of data can be described quantitatively by a single constant,<sup>10</sup>  $\sigma$ , the so-called standard deviation. This quantity is therefore generally accepted as a measure of the accuracy of any series of responses. Roughly, it is only slightly smaller than the average deviation of a series of settings if the subject were to adjust the magnification units. The smaller  $\sigma$  becomes, the steeper is the central part of the curve and the smaller is the threshold value. A small  $\sigma$  would then be associated with a high sensitivity, a large  $\sigma$ , with a low sensitivity. A change in magnification of  $0.6745 \sigma$  would be recognized 50 per cent of the time.

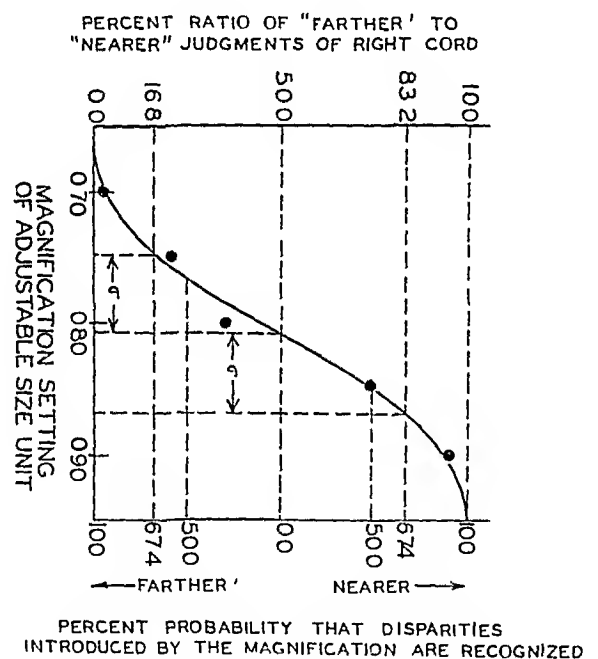


Fig. 3—Typical psychometric curve obtained in determining the stereoscopic sensitivity for the front vertical cords of the space eikonometer to changes in the magnification of the image of the right eye in the horizontal meridian.

For a given set of data, the most probable value of  $\sigma$  and the value of that magnification at the center (the median) of the curve are found by standard statistical methods.<sup>11</sup>

This same method of constant stimuli was also used for studying the sensitivity to differences in size between the images in the two eyes in the vertical meridian.

<sup>10</sup> The curve is the integral of the probability function, expressed by the equation  $y = [1/\sigma \sqrt{2\pi}] \exp(-x^2/2\sigma^2)$ .

<sup>11</sup> The method of least squares is used after attaching weights to the data according to the Muller-Urban process (Woodworth, R. S. *Experimental Psychology*, New York, Henry Holt & Company, Inc., 1938, p. 408-419).

(axis 180), as judged by an apparent rotation of the cross about a vertical axis, and also for studying the sensitivity to changes in the vertical declination between the two eyes introduced by meridional size lenses at oblique axes, as judged by an apparent inclination of the cross about a horizontal axis

*Subjects*—Three subjects took part in the entire series of experiments. The ocular characteristics (for distant vision) of these subjects were as follows

	Uncorrected Visual Acuity	Refractive Error	Phoria at 6 Meters	P. D., Mm
V J E	R E 20/15	+0 12 D cyl, ax 160	1½Δ Exo	62
N W	L E 20/15	+0 12 D cyl, ax 180		
	R E 20/15	+0 25 D sph	¾Δ Exo	60
K N O	L E 20/15	+0 25 D sph	¾Δ RH	
	R E 20/15+	+0 25 D sph (—0 25 D cyl, ax 25	¾Δ Eso	64
	L E 20/15	+0 25 D sph (—0 12 D cyl, ax 10	¾Δ RH	

Two of the subjects (V J E and K N O) had had considerable training and experience with experiments requiring stereoscopic judgments. One subject (N W) had had no previous experience whatever in stereoscopic judgments

RESULTS

*A Stereoscopic Sensitivity to Image Size Differences in the Horizontal Meridian (Axis 90)*—The stereoscopic sensitivity to changes in the relative sizes of the image in the two eyes in the horizontal meridian as observed in an apparent displacement of the two front (green) vertical plumb lines of the space eikonometer was determined, first, as affected by changes in separation of the lines, and, second, as affected by the other configurations in the field of view

It will be clear that, except for small separations, the images of one of the lines will always fall on the peripheral part of the retina of both eyes, whether the eyes are fixed on one or on the other line or in between the two lines. Now, stereoscopic acuity in the last analysis cannot be better than the visual acuity for the same type of test objects. The visual acuity of the eye decreases rapidly from the center of the fovea toward the periphery, rapidly to about 10 degrees and then at a slower rate from there to 60 degrees. While the visual acuity decreases with the peripheral angle, the disparity between the images in the two eyes introduced by magnifying the image in one eye will increase with the peripheral angle (being proportional to that angle)<sup>12</sup>. There was the possibility, therefore, that at some separation of the plumb lines a maximum sensitivity to changes in magnification might be found

Table 2 gives the results obtained for different separations of the lines when the oblique cross was in the field of view and, again, when the

cross was omitted and the front green cords were used alone. These data are also shown graphically in figure 4, in which the abscissas represent the separation of the cords and the ordinates the standard deviation in percentage magnification of the image of the right eye in the horizontal meridian

An inspection of the table shows that, except for subject N W, there was no significant difference when the cords were seen alone or when the other configurations, such as the cross, were included in the field of view. However, for subject N W the difference was significant, for repeated tests gave essentially the same results

For the cords alone, the values of  $\sigma$  found for all 3 subjects were essentially in agreement. For

TABLE 2—Tabulation of Data Which Indicate Stereoscopic Sensitivities for Changes in the Relative Size of the Images in the Two Eyes in the Horizontal Meridian (Axis 90) as Perceived in an Apparent Displacement of the Vertical Plumb Lines of the Space Eikonometer, for Various Separations of the Lines\*

Separation, Visual Angle	Standard Deviations, Percentage					
	With Cross			Without Cross		
	V J E	N W	K N O	V J E	N W	K N O
5 cm (1 2°)	0 130	0 147	0 153	0 118	0 124 0 105 0 081	0 128
15 cm (3 6°)	0 075	0 087		0 079	0 078	
25 cm (6 0°)	0 065	0 054	0 069	0 051 0 063	0 053	0 080
50 cm (11 9°)†	0 056	0 073 0 076	0 056	0 061	0 051 0 052 0 054	0 059
65 cm (15 2 )	0 064	0 113	0 054	0 069	0 057	

\* Values are the standard deviations ( $\sigma$ ) in percentages of image size difference. The visual distance was 2.4 meters.  
† This is the separation usually used on the space eikonometer

separations of the lines from 30 to 60 cm the sensitivities were essentially constant and maximum, the values for  $\sigma$  averaging about 0.055 per cent. For an average separation of 40 cm, this value of  $\sigma$  corresponded to an angular disparity between the two eyes of 187 seconds of arc<sup>13</sup>

These results show that there is no critical separation of the cords for measurement of the size of the image at axis 90 so long as their separations are between 7 and 14 degrees

13 The relation between these data and visual acuity will be discussed in another paper

12 Ames, A, Jr., and Ogle, K N. Size and Shape of Ocular Images. III. Visual Sensitivity to Differences in the Relative Size of the Ocular Images in the Two Eyes, Arch Ophth 7 904-924 (June) 1932

*B Sensitivity to Image Size Differences in the Vertical Meridian (Axis 180)*—Changes in the size of the image in one eye in the vertical meridian can be observed in the space eikonometer by an apparent rotation of the cross about a vertical axis. The right side of the cross appears nearer if the image of the right eye is increased vertically (axis 180). The data were obtained by the method of constant stimuli, the

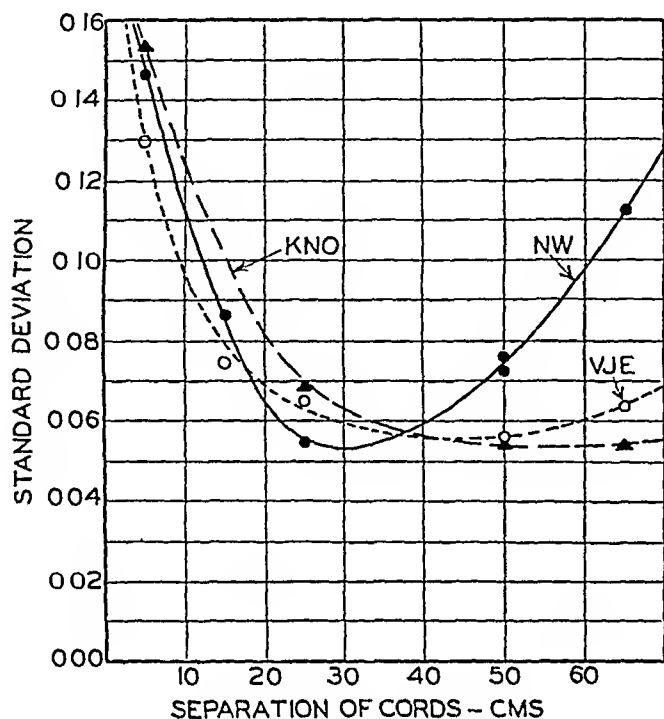


Fig 4—Data for the standard deviations indicating the stereoscopic sensitivities of 3 subjects to changes in the relative magnification of images in the two eyes of the vertical lines of the space eikonometer, for various separations of those lines

changes in magnification being made with the meridional adjustable size unit before the right eye

The essential problem, in addition to determining the sensitivity to the cross as used in the space eikonometer, was to find whether the presence or absence of the vertical cords and the central cord affected the sensitivity

The results obtained by the 3 subjects are shown in table 3. Because a learning trend (training effect) was found for both subjects K N O and V J E, only the results for N W are entirely reliable. The table shows the sequence in which the data were obtained and, also, the repeated data

An inspection of table 3 shows that there is a small increase in sensitivity when the vertical cords are included with the cross in the field of view, but that the separation of these cords has little influence on it. Moreover, the addition of a central plumb line through the cross has little influence except when the other vertical cords are excluded, then a definite decrease in sensi-

tivity is found. The latter was not anticipated, for it seemed as though the vertical cord through the cross would act as an axis for the apparent rotation of the cross

An important result is that the ratio of the sensitivity to image size differences at axis 90 to that at axis 180 is of the order of 4 to 3. This indicates that the same precision of measurement on the space eikonometer cannot be expected for the measurements of image sizes in these two meridians

*C Sensitivity to Changes in Declination*—A magnification of the image of one eye in an oblique meridian introduces, in addition to horizontal and vertical image size differences, a declination of the images of all vertical objects in space. This declination in the space eikonometer causes an apparent inclination of the cross about a horizontal axis through its center

The geared 2 per cent meridional size lenses, described earlier in the paper, can be used to introduce a change in declination to offset any error present without altering the horizontal or vertical image size differences. These geared lenses always introduce an image size difference

TABLE 3—Tabulation of Data Which Indicate the Sensitivities Found for Changes in the Relative Sizes of Images in the Two Eyes in the Vertical Meridian (Axis 180) as Perceived in an Apparent Rotation of the Cross\*

Test Elements	Order in Which Data Were Taken	Standard Deviations		
		Subject N W	Subject V J E	Subject K N O
Cross only	2	0 110%	0 126%	0 099%
Cross and central white line	6	0 117%	0 156%	0 148%
Cross, front and rear cords separation 50 cm	5	0 091%	0 119%	0 124%
	8	0 099%	0 088%	0 085%
Cross, front and rear cords and single, center white cord, separation 10 cm	3	0 086%	0 140%	0 128%
Cross, front cords and single center white cord, separation 50 cm	1	0 081%	0 121%	0 139%
	7	0 085%	0 131%	0 097%
Cross, front and rear cords and single center white cord, separation 64.2 cm	4	0 077%	0 089%	0 102%

\* Comparative data for different configurations used with the cross are shown. The visual distance was 3 meters

in the 45 and 135 degree meridians and have, therefore, no effect on the cross itself. The declination should affect the apparent inclination of the vertical images in the field of view. Because of the cyclofusional movements that usually take place, however, the cross actually appears inclined, the inclination being equal to that expected from the vertical cords. Thus, the sensitivity of the eyes to changes in declination can be measured by the apparent inclination of the cross. It was important to obtain data to show

whether the number of vertical cords in the field of view, especially the central line through the center of the cross, or the presence of triple cords through the center, as indicated in figure 5, affect the sensitivity

The results for the 3 subjects are given in table 4. These data show that for 2 subjects there was a decidedly increased sensitivity to changes in declination when a vertical cord was

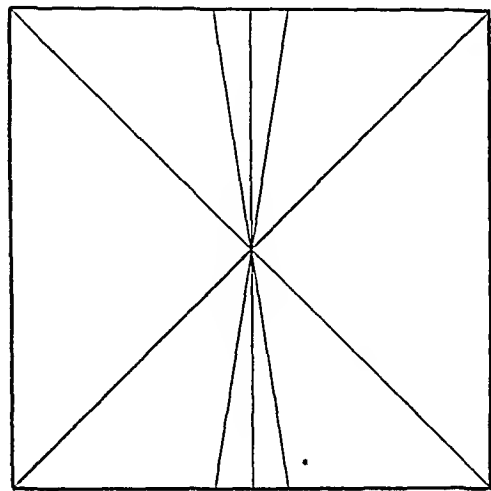


Fig 5—Illustration of the triple cord arrangement sometimes used in the space eikonometer. These cords lie in the plane of the cross and cross at its center.

placed through the center of the cross. With the triple cord arrangement, there was a tendency to even higher sensitivities. For the third subject K N O, it did not make any difference. The explanation for this seems to be that the last subject was careful to use all possible spatial clues and compensated for the lack of the central

TABLE 4—*Tabulation of Data Which Indicate the Sensitivities Found for Changes in Declination Between the Two Eyes as Perceived in an Apparent Inclination of the Cross\**

Test Elements	Order in Which Data Were Taken	Standard Deviations		
		Subject N W	Subject V J E	Subject K N O
Red cross, front and rear cords, triple center white cords	1	0.106°	0.076°	0.060°
Red cross, front and rear cords, single center white cord	2	0.104°	0.109°	0.081°
	5	0.070°	0.084°	0.077°
Red cross, front and rear cords, no center cord	3	0.194°	0.170°	
	6		0.187°	0.075°
Red cross, single center white cord	4	0.092°	0.090°	0.074°

\* Comparative data for different configurations used with the cross are shown. The visual distance was 3 meters.

cord, while the other 2 subjects, who had become accustomed to it, were not as careful to look for substitutes before making the judgments. A repetition of the third experiment of the sequence for subject V J E demonstrates the repeatability of the data. While there is evidence of some

training effects in the results for N W and V J E, it does not appreciably affect the interpretation of the data. The order of magnitude of these data is striking, for they indicate that in the majority of times in which the stimuli were presented the eyes were able to discriminate a declination angle of less than 0.1 arc degree (6 minutes of arc).

*D Modified Cross Configuration*—Other configurations of the cross are, of course, possible, and even practical for certain purposes.<sup>4</sup> Consider for example, the Maltese-like form shown in figure 6, consisting of four stretched cords all passing through the center of the configuration, each pair making an angle of 5 degrees with the diagonals of the square frame.

When a change in declination is introduced, the two “vanes” formed by the same two cords appear to turn in directions opposite each other about the 45 (or 135) degree axis (not unlike the blades of a propeller).

A study of the sensitivities of the 3 subjects to changes in declination as perceived on this cross was made as previously described. The results are shown in table 5. For comparison,

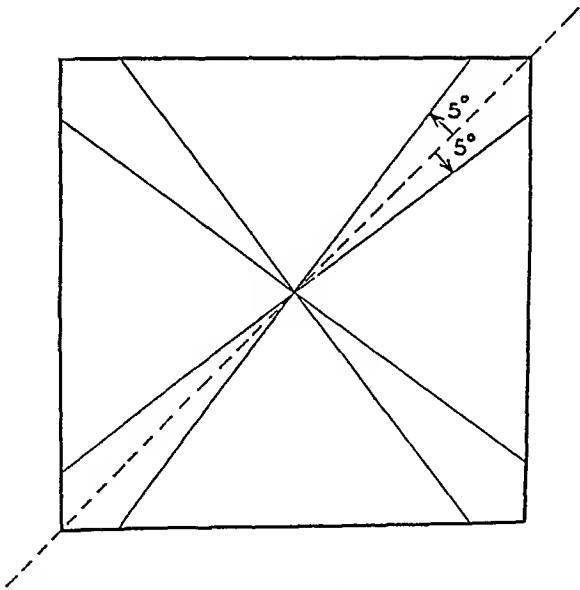


Fig 6—An alternate form of the cross which is highly sensitive to changes in declination.

the sensitivities found for the configuration of the regular cross are also included. The sequence of experiments is indicated in parentheses.

In the space eikonometer with the Maltese cross, the elements consist of the front and rear cords together with the cross, just as the regular space eikonometer is made up of simple cross, front and rear cords and single central cord. For this reason, the second and third horizontal columns should be used in comparison of the sensitivities with the configurations of the two

crosses The results definitely show that a much higher sensitivity can be secured with the Maltese cross

No explanation can be given for the increased sensitivities found for 2 of the subjects (V J E and K N O) when the front and rear paired cords were added as compared with those found with the Maltese cross alone

TABLE 5—*Tabulation of Data Which Indicate the Sensitivities to Changes in Declination as Recognized in the Apparent Distortion of the Maltese-Like Cross Configuration at a Fixation Distance of 3 Meters*

Test Elements	Standard Deviations		
	N W	V J E	K N O
Maltese cross only	0 070° (1)*	0 098° (1) 0 091° (2)	0 079° (1) 0 083° (3)
Maltese cross, front and rear paired cords	0 079° (2)	0 066° (3)	0 060° (2)
Simple (two cord) cross, front and rear cords, single center white cord	0 087°	0 105°	0 096°

\* The numerals in parentheses indicate the order in which the data were taken

*E Sensitivity Experiments on the Space Eikonometer for Near Vision*—Test elements of the space eikonometer, proportionally reduced in size, were also set up for measurements to be made at near vision (40 cm) These elements were placed in a reading position normal to a visual plane with the eyes directed 20 degrees below the horizontal plane Single fibers of triple strand silk thread were used to make the various configurations The illumination at near vision

TABLE 6—*Tabulation of Data Which Indicate the Binocular Sensitivities to the Space Eikonometer Test Elements for Near Vision and, for Comparison, the Equivalent Data Obtained for the 3 Meter Test\**

Regular Space Eikonometer		Visual Distance	
Subject	Sensitivities for	40 Cm	3 Meters
K N O	Size differences, horizontal	0 087%	0 056%
	Size differences, vertical	0 096%	0 097%
	Declination change	0 205°	0 096°
N W	Size differences, horizontal	0 111%	0 074%
	Size differences, vertical	0 136%	0 085%
	Declination change	0 164°	0 087°
V J E	Size differences, horizontal	0 089%	0 062%
	Size differences, vertical	0 213% 0 172% 0 239°	Av 0 131% 0 192%
	Declination change		0 105°

\* The values are the standard deviations  $\sigma$  obtained from an analysis of the method of constant stimuli

was the same as that used at 3 meters A large piece of black velvet placed 60 cm behind the test elements served as background All other parts of the instrument were the same as those previously described except that the axes of the

test lenses were converged for the 40 cm distance

The results of the same subjects in this test for near vision are shown in table 6, together with the results with the 3 meter instrument, for comparison

In all cases but 1 (K N O for axis 180), the sensitivities for near vision were found to be lower than those for distant vision For the horizontal and vertical meridians, the ratio was of the order of 4 to 3 For sensitivities to changes in declination, however, the test for near vision was only half as sensitive as the 3 meter test Again, the sensitivities for axis 90 (horizontal meridian) were definitely higher than were the sensitivities for axis 180 (vertical meridian) <sup>14</sup>

# SUMMARY

This paper presents the results of a study of the stereoscopic thresholds of response for the space eikonometer With this instrument, the aniseikonic error can be measured by the apparent orientation of the test elements as perceived by stereoscopic space perception Three components of the aniseikonic error are measured the image size differences in the horizontal meridian (axis 90) and in the vertical meridian (axis 180) and the error introduced in the normal declinations between the two eyes The last will occur if the aniseikonic error includes a meridional image size difference at an oblique axis

The stereoscopic sensitivities, as measured by the thresholds of discrimination, of 3 observers were determined by the method of constant stimuli under carefully controlled conditions and were expressed in terms of the standard deviation For distant vision (3 meters) the results were as follows

1 For the horizontal meridian (axis 90) the aniseikonic error is detected by an apparent difference in distance of two vertical plumb lines For the clinical instrument, in which the lines subtend a 10 degree field (50 cm, separation at 24 meters), the standard deviation was of the order of 0.05 per cent in magnification of the images in the two eyes This corresponds to an angular disparity between the images of the two eyes of 21 seconds of arc Since the recognition of this disparity depends on the visual acuity of the retina at 10 degrees from the fovea, 21 seconds of arc is significantly high

14 Polaroid vectographs of the test elements were also substituted for the actual threads and the sensitivities determined for both distant and near vision In general, the sensitivities found were of the same order as those given above



2 For the recognition of changes in the relative sizes of the images in the vertical meridian (axis 180), as detected in an apparent rotation of an oblique cross about a vertical axis, the standard deviation was of the order of 0.07 per cent in magnification of the images in the two eyes

3 The sensitivity to changes in the vertical declination angle between the images in the two eyes, perceived in an apparent inclination of the oblique cross about a horizontal axis, as measured

by the standard deviation was of the order of 0.1 degree

Somewhat lower sensitivities (higher thresholds) were found for near vision, especially for the changes in the declination angles

The results of this study of sensitivities emphasize the accuracy of the space eikonometer for the detection and measurement of aniseikonic errors

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# CLINICAL DIFFERENTIATION OF EMBOLI IN THE RETINAL ARTERIES FROM ENDARTERITIS

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This paper is the summation of the study and correlation of many cases of sudden blindness caused by the abrupt closure of the central retinal artery, or a branch of the same. The conclusions have not been collected haphazardly but are presented after repeated examinations of the photographs and clinical histories. Textbooks, those proverbial exponents of repetitions, ancient and modern, rarely guide the student through the maze of generalizations to the correct diagnosis of changes in the retinal vessels. This is not said to disparage, for the compilation of any good textbook is an engaging, time-consuming task, but, rather, to ask the reader to start with an open mind for the reception of a new clinical differentiation between embolism of the central retinal artery and endarteritis. However, before the clearly defined groups are separated, it is essential to remember that there are cases of combined lesions, as, for instance, those of patients with severe hypertensive retinal changes who suddenly go blind as the result of a superimposed embolism. A source of constant confusion is spasm of the retinal arteries, which is, to my mind, a loosely applied term. Spasm plays an important role in some cases, and for that reason will be the subject of another paper, to be presented elsewhere.

The scope of this paper is strictly limited, and although pathologic proof is not presented, a sufficient number of reports are now available to warrant the conclusions here expressed. To emphasize further the visible differences in these cases, 2 cases of complete embolism are reported and photographically recorded from a few hours after the primary loss of vision to the terminal stage of complete optic nerve atrophy, with a narrow, threadlike retinal arterial tree. Particular attention is paid to the changes which at the onset take place in the circulation. These are greatest in the superior temporal vein, less frequent in the corresponding artery and still more rare in other branches. The alterations in the size, color and surface of the macular area, and the extent and intensity of the retinal edema are considered, and attention is drawn to the rapidity with which the disk

becomes pale, loses the fine vessels on its surface and, finally, becomes white, with a shallow, complete atrophic cup. It must be repeated again and again that the retina is like the human body as a whole, and that vascular changes of similar intensity produce variable results. An unusually careful scrutiny of every case is necessary to observe the changes here described and few ophthalmologists record their observations in sufficient detail to be of value comparable to that of serial, color photographs of the fundus, and for that reason conclusions based on the analytic review of years of written reports are not always convincing. After the war, it will be possible to publish more colored reproductions, so that all who wish may examine them in the detail which they deserve.

## ILLUSTRATIVE CASES

CASE 1—A typical ophthalmoscopic picture of embolism, from eighteen hours after the primary obscuration of vision to the formation of complete optic nerve atrophy is well illustrated by the case of C N, a 34 year old married man, who, twelve years before the beginning of his blindness, had acute rheumatic fever with endocarditis. Through the intervening years, he was seemingly free from any gross manifestations of heart disease and had never had any trouble with his eyes until Nov 30, 1942, when suddenly the vision of the left eye began to fail and in one hour he was blind in that eye.

He was examined eighteen hours after the onset. Vision in the right eye was 20/30, and with correction of  $-0.50$  D sph it was 20/20. The eye was normal externally, and there was evidence of pathologic changes in the fundus. The retinal vessels were completely normal.

In the left eye, vision was limited to faint perception of light. The pupil was 3.5 mm, regular and active. The media were clear, and the disk was sharply outlined. An oval zone, including the disk and extending a short distance beyond the macula, was both elevated and cloudy. The haze was greatest and the elevation most marked in the circummacular area, in the center of which was a small, bright red spot. The retinal veins were narrower than normal, and in places, particularly in the inferior temporal branch, the vessel was greatly contracted in portions of its course and slightly dilated in others, so that it looked like a streak hemorrhage, starting at the margin of the disk and extending toward 4.30 o'clock. The superior temporal veins showed distinct interruptions of the blood stream with spaces between the red cell groups, which

were pulsating, with a definite motion toward the disk. The arteries were definitely smaller than when the patient was first examined.

Twenty-four hours later, the edema was greater about the macular area, and the red spot was decreased in size and brightness. The haze surrounding the disk was increased in intensity but not in extent. More blood was passing through the superior temporal vein, but there were many interruptions in the stream, and the propulsion toward the disk was more easily discernible.

Two days later, the edematous perimacular swelling was flatter, the macular spot was brownish yellow, and the circulation through the superior temporal vein was almost completely reestablished.

One week later, there was narrowing of the lumen of the arteries, especially on the disk. There was no interruption in the current of the superior temporal vein and very slight reduction in the caliber of the inferior temporal vein. The disk was slightly paler than it had been, and the edema was decidedly decreased. From the macula there were radiating dark lines, breaking the clouding into segments. The red spot was larger than the previous week.

choroid. The veins were about one-third their normal size and the arteries were thin threads devoid of plaques along their walls, but the macula was pink, with a very few pinpoint spots. The perimacular area was dark, slate gray. The eye was blind.

It is possible to theorize as to the cause of the embolus, for the patient had had endocarditis and from the valvular vegetations a plug may have broken loose. No other suggestive cause was discovered either in the history or on physical examination.

**CASE 2**—In this case the patient was grossly devoid of cardiac disease. She had lost 30 pounds (13.6 Kg) in the past two years, without any assignable cause. Suddenly, without any premonition, darkness spread over her left eye, and within eight hours the first photograph was taken.

The patient, a 65 year old woman, was first seen Feb. 6, 1942, when the vision in the right eye was 5/200, corrected to 20/20. The fundus was entirely normal.

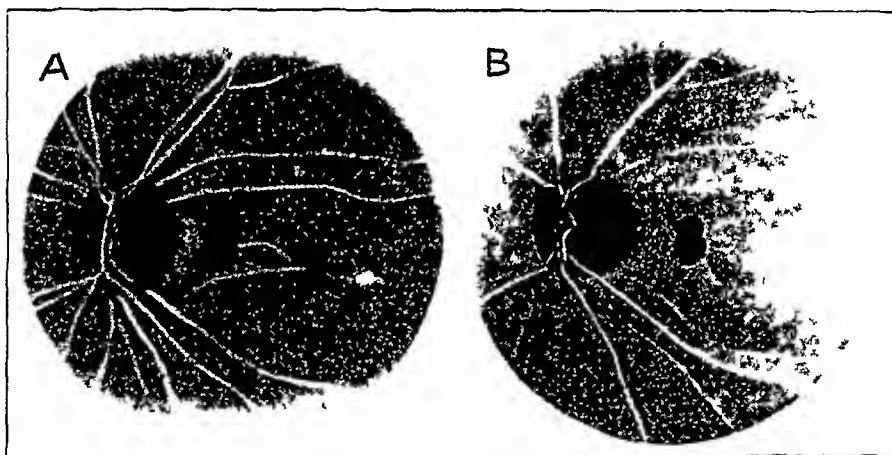


Fig. 1 (case 1)—*A*, embolism of the central retinal artery, with interrupted blood stream in the superior temporal vein and artery, oval edematous area and small macular red spot.

*B*, fundus seen in *A* five months after occlusion, showing white disk, narrow veins, attenuated arteries and granular macula.

At the end of another week, the disk was distinctly pale. The caliber of the superior temporal vein was not uniform. The edema about the macula was less, and the red spot was larger.

Twenty-seven days later, the pallor of the disk was increased, the swelling of the retina was decreased, and the formerly raised, gray macular region was flat and granular white. The granules were best seen over the dark reddish center, where they appeared as yellowish, pinpoint specks. The edema about the disk had entirely disappeared, and the lumen of the superior temporal vein, as evidenced by the width of the blood column, was reduced.

At the end of ten days, the atrophy of the disk was manifest by its extreme pallor and the shallow excavation. The arteries were narrower than before, and the veins were constricted. There was no white or cloudy swelling about the macula, which was flat and dull gray. The fine, previously mentioned specks persisted.

Three months later, the appearance was typical of true embolism: a white disk, faint peripapillary pigmentation and, to the temporal side, partially absorbed

Vision in the left eye was limited to faint light perception. The pupil was 3 mm and reacted to light. The media were clear. The disk was clearly outlined, although partly covered by the retinal edema, which was very thick. A small uninvolved section of the retina, to the lower temporal edge of the disk, supplied by a cilioretinal artery, was normal pink. The edema was greatest about the macular region and extended slightly to the nasal side of the disk. The macula was dark red. There was interruption of the blood stream in the superior temporal artery, the parallel-ling vein and the inferior temporal artery.

The next day, the retinal edema was more uniform in texture and more dense. The macular spot, although still red, was reduced to about one eighth of its previous diameter. The interruptions in the blood stream in both the superior temporal artery and the vein were very evident. The blood cells were in constant oscillation, with motion toward the disk. The breaks in the blood current in the inferior temporal artery were less distinct.

Ten days later, the disk had lost some of its normal pink color. The edema was notably decreased but still

greatest about the macular region, where the central spot was twice its former size. The interruption of the blood stream was marked in the superior temporal vein, although there were no clear spaces between the cell groups. The circulation was restored in the artery. The volume of blood in some of the branches extending from the superior temporal vein down to the macula was unequal. The arteries showed a decided decrease in caliber, they were partially covered by the edema, and the inferior temporal branch had gray walls.

On the sixteenth day, there were striking changes, the disk was pale, the edema was practically confined to the perimacular region, the red spot had not increased in size since the last visit, the interruptions in the blood stream were absent and the vessels above the fovea were clearly seen.

On the twenty-fourth day, the only region in which the retinal swelling remained was about the macula, where the retina was almost homogeneous gray and nearly flat. Several fine, pinpoint specks were found in the area, and, as with all such lesions, they were best seen on the pink background of the macula. The arteries were more shrunken, so that in places they could be traced only with difficulty. There was no

responding to that region. It will be recalled that this peripapillary clear portion has been referred to by other writers, and for that reason this evidence of its existence is presented.

An embolus of a branch of the retinal artery can be recognized ophthalmoscopically and proved pathologically. Clinically there are two types of embolus: one, which remains practically unchanged in size, and the other, in which there is an elongation as the plug becomes larger or the vessel proximal to it becomes thicker.

**CASE 3**—An example of the enlarging plug is that of a woman 68 years old who had been under my observation for many years, with normal fundi. Twenty hours previous to the examination, on Oct 20, 1938, she noticed a blur before her right eye and in a few minutes found that she could see only the lower portion of the objects at which she looked. Her only pertinent illnesses had been recent tonsillitis and chronic pyelitis. The systolic blood pressure was 180.

Vision in the affected eye, the right, was 18/200. Externally the eye was normal. The disk was clearly

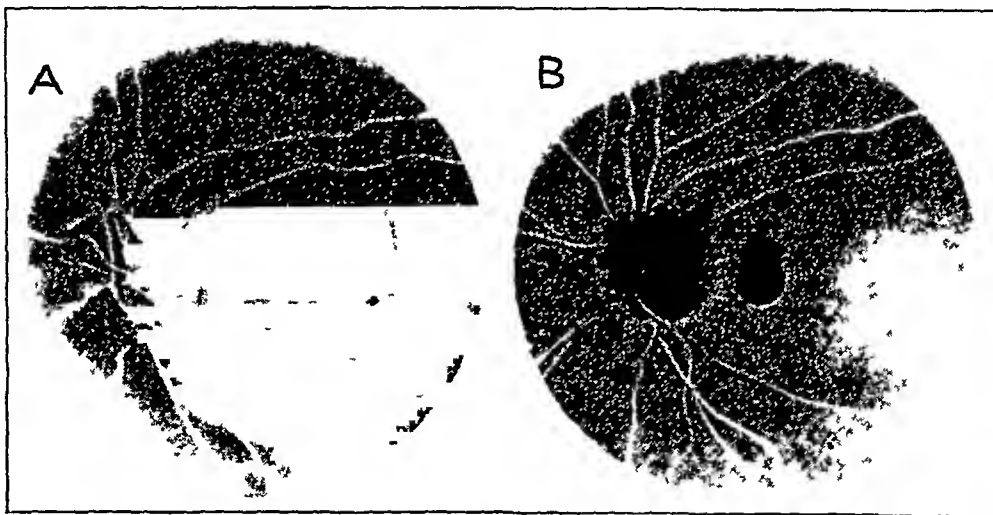


Fig 2 (case 2) —*A*, embolism of the central retinal artery, with interrupted blood stream in both the superior temporal vein and the artery, broad oval of thick edema and small macular red spot.

*B*, fundus seen in *A* two months later, showing optic nerve atrophy, narrow arteries and veins and granular macula.

interruption of the blood stream. The disk was white and devoid of any fine vessels.

Thirty-six days after onset, the perimacular region was dark, flat and covered with scattered, yellowish, pinpoint specks. The macular area was larger than it had been, the arteries were smaller, with faintly visible gray sheathing.

On the sixty-first day, the disk was white, with a circumpapillary arc of pigment. The retina was mottled and dark, with a few specks between the macula and the disk. The arteries and the veins were decidedly smaller. There was complete loss of vision.

The color of the fundus background, darkly mottled, the age of the patient and the general conformation gave a different terminal picture than that noted in case 1. The small almost triangular, area of the retina proximal to the disk at 3 30 and 4 30 o'clock was never edematous and never lost its color. This explains the retention of the very small field cor-

outlined, with a small central excavation. The retinal vessels in the upper half of the fundus were normal. In the lower branch of the artery, inferior to a bifurcate division, there was a white, bright, occluding plug, which seemed very slightly wider than the artery and perceptibly longer than wide. Distal to the occlusion, the artery was reduced in size but not abruptly collapsed, and there was no interruption in the blood stream. The portion of the fundus supplied by this artery was white, with an irregular outline extending to the lower portion of the macular area as a curved white border. This edema extended only slightly beyond the nasal side of the disk. There was a defect in the superior nasal quadrant of the visual field.

Four days later, there was no change either in the field or in the central visual acuity. The retina was unchanged in color and the plug unaltered in size.

At the end of fifty days, the arterial plug was slightly longer than when first noted, and the retinal edema had disappeared.

On the ninety-second day, vision was 20/100, corrected to 20/20 with +1.75 D sph. The sector defect

in the field persisted. The retina was of normal color. The vascular plug was about three times its original length, and the vessel distal to it remained unchanged in size and color.

In this case of sudden occlusion of the inferior retinal artery, the white plug was seen twenty hours after the onset, and at that time, when the localized retinal edema was pronounced, there was no interruption of the blood stream. Months later, when the plug had extended down the artery to more than twice its primary size, the vessel wall was unchanged, neither gray nor covered with white plaques.

In another case of embolus of the inferior branch, the white plug was grossly larger than the vessel, and the narrowing of the artery was very conspicuous.

**CASE 4**—The patient, a 53 year old merchant, was not seen until a week after the sudden obscuration of the vision of the right eye.

A week later, the retina remained the same and the plug narrow.

Ten days later, the plug was practically unchanged, and the artery remained narrow.

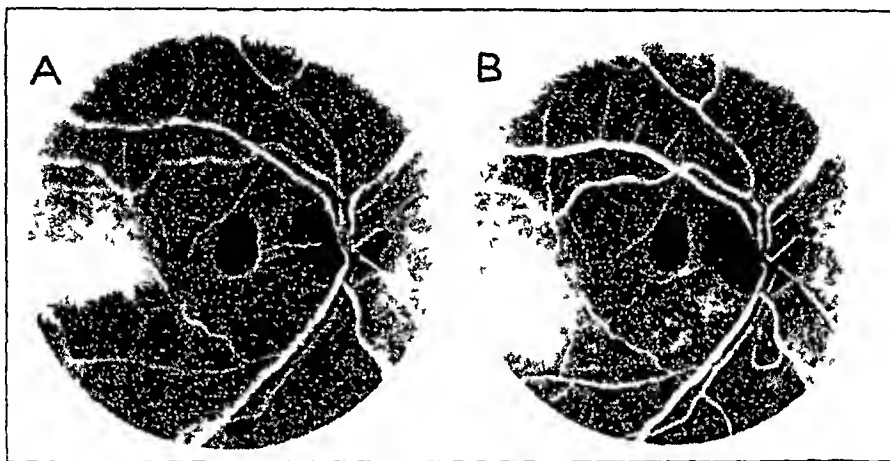
At the end of eighteen days, the retina was of normal color.

Three months later, vision was 10/200. On the mottled retina the vessels were clearly seen, the inferior temporal artery was narrow on the disk and a short distance beyond the margin. The embolus was of the same size as when first seen. The lower half of the disk was pale, and the visual field had not enlarged.

In this case no systemic disease was discovered, no source of an embolus was uncovered, and there were no gross vascular changes. His systolic pressure was 140 and his diastolic pressure in proportion.

This case was one of embolism, of unknown origin, permanently destroying the upper half of the visual field.

The first patient, with a branch occlusion, was seen early enough and followed at sufficiently short intervals for any breaks in the blood stream.



**Fig 3 (case 4)**—*A*, embolism of the inferior temporal artery, with a visible plug in the artery on the disk. The vessel distal to the plug is narrowed. Cloudy retinal swelling of the inferior temporal quadrant is present.

*B*, fundus seen in *A* three months later, showing pale inferior temporal quadrant of the disk. The plug in the artery is unchanged, with narrowing of the inferior temporal artery. Complete resolution of the retinal edema has occurred.

Vision in the right eye was 5/200, corrected to 10/200 with +1.50 D sph. Externally the eye was normal. The disk was almost round and was clearly outlined. Just inferior to the bifurcation of the lower branch of the central retinal artery, the temporal division was closed by a small, glistening white mass, wider than the diameter of the vessel and about twice as long. Immediately distal to the plug there was marked contraction of the artery, which was evident for a distance of  $\frac{1}{3}$  disk diameter, where it gradually widened, but not to the diameter of the superior branches. The vessels in the upper half of the fundus were normal in relative size and distribution. Some thick, white, round-bordered areas of retinal edema outlined the lower margin of the macular region. The inferior vein was unchanged, and there was no discontinuity in the blood flow. The edema was scarcely perceptible in most of the lower half of the retina. There was an almost complete loss of the upper half of the visual field.

On June 26, 1944 the white retinal areas were decidedly less evident.

to have been observed if they were present. The second patient did not come under observation for several days, too late for interruptions to be evident. However, up to the time of this report I have neither photographed nor seen a segmentation of the blood column in a case of branch block.

To appraise accurately the difference between an occlusion in a presumably normal artery and one in a previously damaged vessel, it is necessary to recheck carefully the details and, when possible, the photographs. The following cases of endarteritis will demonstrate the value of such a study.

**CASE 5**—The first case was that of a man 51 years of age who, about twenty-four hours before I saw him, noticed a cloud cover his right eye. A few seconds later, he covered his left eye and found that his right eye was sightless.

On Sept 2, 1937 the right eye was normal externally. The fundus was white with the exception of the disk and macular region. The retinal edema was of variable thickness, so that the effect was one of a dappled, milky background. The margins of the disk were ill defined because the swollen retina bulged over the edges. There was a small central excavation. The retinal veins were reduced in caliber, in some places they were partly covered by the edematous retina, and in others they were dark red, patent streaks. The arteries were small, especially about the disk, and, like the veins, they were often completely hidden in the retina. The vessels about the red macular area stood out as pink threads on a white background. There was no intermittent current in either the arteries or the veins. The walls of the artery were gray, particularly the inferior temporal branch near the margin of the disk.

Two weeks later, the pallor of the disk was greater, the retinal edema was less, and the walls of the nasal branches of the artery were more manifest. On the inferior temporal artery, almost directly below the disk, there was a white plaque. Distal to this lesion the vessel was a bloodless gray thread for a distance of about  $\frac{1}{2}$  disk diameter, at which point the blood stream regained its full volume.

Two months later, vision was limited to perception of fingers at 1 foot (30 cm) in a very small temporal field. The pupil was 4 mm, regular and active. The white disk was clearly outlined, with an arc of partial depigmentation at the temporal margin. The arterial tree showed prominent sclerotic patches, the longest one was in the superior temporal branch, but there were others along the inferior division. Several of the other branches were white walled and all of them decreased

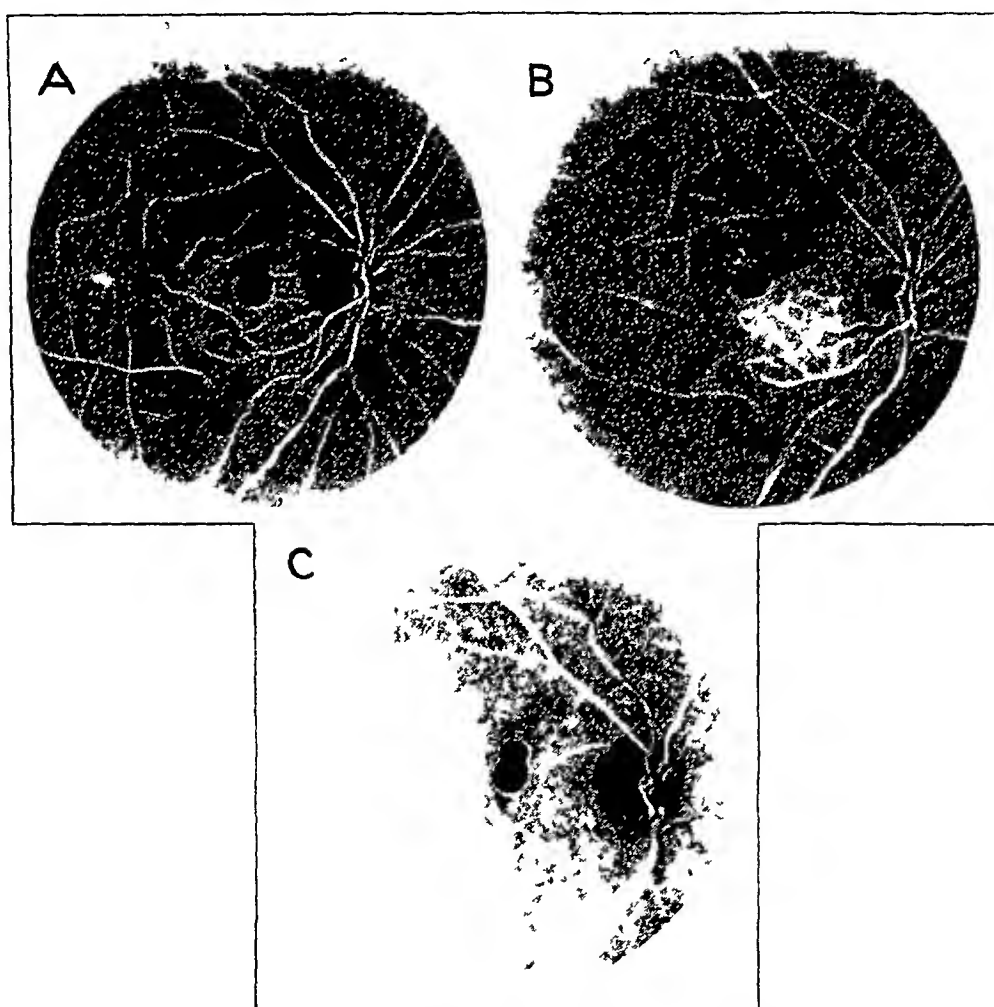


Fig 4 (case 6) —A (March 14, 1942), endarteritis of the central retinal artery, with retinal edema twenty hours after onset. The clear portion is supplied by the cilioretinal artery. Changes in caliber appear in the arteries. The macular red spot is of normal size.

B, fundus forty-eight hours later. Retinal edema is much more extensive and intense, the macular red spot is a mere dot, and arterial changes are especially pronounced in the inferior temporal branch.

C, fundus twelve weeks after onset, showing complete optic nerve atrophy, very irregular caliber of the narrow arteries and white plaque in the wall of a sclerotic vessel. This is terminal stage of endarteritis.

The patient had not been under medical supervision, although his blood pressure was 210 systolic and 140 diastolic.

On the following day, there was a decrease in the size of the macular red spot.

Twenty-two days later, the edema of the retina had subsided but was still evident near the temporal side of the disk. The gross changes in the arteries were narrowing of the lumen and increased visibility of the wall with beginning plaques, best seen near the inferior margin of the disk. The macular area was red, granular and flat and the perimacular circulation well defined

in size. The veins were smaller than normal. The macula was dark, with fine granular spots, and there was complete atrophy of the optic nerve, with a white nerve head. The patient died March 19, 1940.

The condition in this case was considered endarteritis for several reasons: first, the widespread primary edema, which involved the entire visible retina; second, the demonstrable old vascular changes, which were found immediately after the blindness and therefore were present



before the complete occlusion, and, finally, and most conclusively, the gross, white arteriosclerotic plaques, which were very different from the pale, yellow emboli, not only in their extent but in their position on the artery wall rather than occluding the lumen of the vessel

The final case is instructive, for although it terminated in complete optic nerve atrophy, with white-walled arteries, there were peculiarities in the blood supply, the intensity of the retinal edema and the manner of its resolution

**CASE 6—W E T**, a 56 year old man, suddenly lost the sight of the right eye about twenty hours before the first examination

On March 14, 1942, the vision of the right eye was limited to questionable perception of fingers. The pupil was 3.5 mm and reacted promptly to light and in accommodation. The disk was clearly outlined and was of normal pink color, with a moderate-sized central excavation. An area to the temporal side of the disk, supplied by a cilioretinal artery, was pink.

The retinal edema was in places a dense white and in others appeared as a uniform gray haze. The macular red spot was of average size and clearly outlined. The veins were of normal size and distribution. The arteries in many places covered by the gray retina, showed marked variations in caliber without segmentation of the blood column.

The patient was a stout, red-faced, plethoric person who had had high blood pressure for an unknown number of years. During this time he had two cerebral vascular spasms, when for a few days he was partially paralyzed. The blood pressure was 230 systolic and 120 diastolic. There was a slight trace of albumin. The roentgenogram disclosed a wide, tortuous aorta. The Wassermann reaction of the blood was normal.

The changes which took place in forty-eight hours were striking. The white clouding of the retina was more pronounced, and in places there were whiter, elevated mounds, of great density. The macula was a mere pink dot. Along the side of some of the finer arteries there were delicate streak hemorrhages. All of the retinal vessels were smaller than normal.

Three days later, the thick, white retinal cloud was intense. The disk was still pink. The arteries showed an increased visibility of the walls, most evident inferiorly. The macula was only a pinpoint, and the vessels surrounding the upper portion of it had an irregularity of lumen which could easily be mistaken for an interruption of the blood stream.

At the end of another week, the edema was disappearing. It was greatest about the macula, with broad side wings above and below it. The macular red spot had doubled in size but was smaller than when first examined. The disk was beginning to lose its color.

A week later, the retinal edema was less, remaining greatest about the macula and in a crescentic zone outlining the distribution of the superior temporal artery. The macula was red. There was an increased visibility of the artery, with considerable decrease in the lumen of several branches, especially the inferior temporal ones.

After another seven days, the disk was definitely white, the edema was decreased in intensity, and the macula remained a red spot.

Twelve weeks from the onset, there was an atrophic depression of the white disk, with irregular surrounding pigmentation. Arteriosclerotic white plaques were visible

along the arteries, greatest over and proximate to the disk, as usual. Both the arteries and the veins were very narrow, the former mere threads. The macula was slightly redder than the surrounding fundus, and there were a few white granular specks on and about it.

This case illustrates the arteriosclerotic plaques, the density of the retinal edema and the manner of its disappearance in a patient with hypertension who died shortly afterward, from a cerebral vascular accident.

#### SUMMARY

In cases of embolism of the central retinal artery, an early sign is the interruption of the blood stream, usually in a vein, although it may be in both a vein and an artery. The site of predilection seems to be the superior temporal divisions. The zone of retinal edema is rather sharply defined to an oval, which includes the disk and the macula and rarely, if ever, extends more than 1 disk diameter beyond either or both. The size of the macular so-called cherry red spot, a misnomer, depends on the choroidal blood supply, on the type of fundus, whether albinotic, mottled or some other form, and on the intensity of the edema. At the onset the macular spot is unchanged in size, but as the retinal edema increases, it becomes smaller and smaller and may entirely disappear. Later, as the edema subsides, the macula becomes larger and larger. With the disappearance of the edema the color of the fundus is more or less uniform, and many fine, yellow-white, pinpoint dots are scattered over it. These are best seen where the fundus is reddest—the macular region.

Coincident with the decrease in the edema there is a progressive narrowing of both the veins and the arteries. The arteries finally become mere white threads, devoid of plaques on their walls. It is probable that in the case of a true embolism there are no retinal hemorrhages. At a variable time after the plugging of the artery, the optic nerve begins to lose its normal pink color, and eventually it becomes a sharply demarcated, atrophic, white disk.

In cases of endarteritis there is at the onset of the blindness always some evidence of pre-existing arterial disease—an increased reflex from the vessels, increased visibility of the wall, irregularity of caliber, indentation of veins, minute aneurysms, exudates, hemorrhages or other signs of arteriosclerosis and hypertension. The interruption of the blood stream is much less constant than in embolism, and often what seems to be a fragmentation is a beaded vessel or one covered by the edematous retina. The retinal edema

is thicker than in the case of embolism and is often dappled, with patches of increased whiteness in the involved area. The edema is usually throughout the entire visible retina, and is not limited to a posterior oval region.

An embolism may be superimposed on endarteritis, and after the primary retinal edema has subsided, a minute white plug may be found in a distal branch of the artery.

#### CONCLUSIONS

In cases of embolism of the central retinal artery, the arteries become mere threads and the veins greatly reduced in size. The wall of the artery may be visible. The optic nerve is white, completely atrophic and sharply outlined.

In cases of endarteritis, the arteries are rarely as small as those found with embolism. There are always white plaques along their walls. The optic nerve atrophy is similar to that of embolism.

The retinal edema from embolism is limited to an oval area, which includes the disk and the macula. The edema in endarteritis usually involves the entire visible fundus.

These conclusions, based on the intensive study of photographs and fundi, are offered for serious consideration and are advanced in the hope that other observers may confirm them, so that eventually embolism can be more readily differentiated from endarteritis.

344 State Street

# AN UNUSUAL CASE OF HODGKIN'S DISEASE

## SECOND REPORT <sup>†</sup>

JOHN WAITE AVERY, M D

AND

J W WARREN, M D

HOLLYWOOD, CALIF

In a previous issue of the ARCHIVES, we made a preliminary report on the case of Mrs M W, then aged 50, in whom the disease involved the lymphatics of the bulbar conjunctiva of both globes, as well as various somatic glandular structures

A lump in the cheek was first noticed by the patient in 1935 and was soon followed by flat, reddish growths on the eyeballs

They were not tender and did not respond to medical treatment. About one year after their appearance they were excised, but in six months they again appeared on both globes in the same locations. Invasion of other glands was increasing, the patient was weak and losing weight, vision was poor and painful, and she had pronounced nasal occlusion.

The patient came under the care of one of us (J W A) in April 1940 and was referred to the Malignancy Committee of the Hollywood Presbyterian Hospital. A biopsy of tissue from the inguinal glands was made. The committee and the laboratory concurred in the diagnosis of Hodgkin's disease, after Wassermann (Kolmer) and Kahn tests and an agglutination test for brucellosis gave negative results.

In May and June 1940, Dr J W Warren gave a series of fifteen roentgen treatments to the globes and the affected glands, and a second series, of ten treatments, in November and December of the same year.

Ten days after the first roentgen treatment the ocular lymphoid growths were thinner and somewhat bleached. In another eight days the eyes were markedly better, and all enlarged glands smaller. Nasal obstruction was no longer felt subjectively, and the pharyngoscope showed an open epipharynx. The improvement was general and constant.

Frequent examinations of the eyes over a period of a year showed no unfavorable changes. Normal vision was maintained with a moderate correction. "By March 21, 1941, the only glandular enlargements palpable were the one on the left cheek, which was small and was felt only on deep palpation, a cordlike condition of the upper anterior cervical chains, small but palpable, and a few small, irregular stained areas on the left globe at the site of the extensive lymphatic infiltration."

Since the date of this report, November 1941, we have kept regularly in touch with the patient. In 1942 no roentgenographic or other treatments were given.

In May and June 1943, ten roentgen treatments were given to the somatic glandular areas only, not to the eyes. There was no evidence of a return of the former pathologic process, but the patient was somewhat asthenic, and the gastrointestinal tract was not normal. The latter conditions were finally determined to be caused by overwork, under unfavorable shop conditions.

A change to better surroundings brought a rapid improvement in her general health, including a gain of 15 pounds (68 Kg). The patient remains in excellent health and has had only a few slight colds the past four years.

There has never been the slightest tendency to a recurrence of the lymphatic involvement of the bulbar conjunctivas. Both scleras are white, but the left, at the site of the former growth, appears slightly pebbly, and two small vessels traverse this area. The former leukoma, near the center of the left cornea, is now a faint nebula measuring about 3 by 4 mm. The nose and throat are in good condition. There still remains a small infiltrate in the left buccal muscle, freely movable, painless and found only on deep palpation.

The upper part of each anterior cervical chain of glands is slightly palpable only as a thin cord, probably the result of a sclerotic change, and the posterior chains cannot be felt.

The Malignancy Committee of the Hollywood Presbyterian Hospital reports as follows:

"Examination reveals no evidence of the former Hodgkin's disease. The eyes seem clear. There is still a small residual lump in the left cheek. Palpation of all the superficial lymph nodes in the groins, axillas and elbows gives negative results. There seems to be no palpable enlargement of the spleen."

The purpose of this report is not to offer a new therapeutic approach to Hodgkin's disease but simply to record an apparently unreported invasion of unusual lymphatic areas, to which roentgen radiation was applied, successfully thus far, and without injury to the delicate structures of the globes.

We hope to report again, perhaps after several more years.

7166 Sunset Boulevard  
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<sup>†</sup> Report as of Dec 18, 1944

1 Avery, J W, and Warren, J W. An Unusual Case of Hodgkin's Disease. A Preliminary Report, Arch Ophth 27 1019 (Dec) 1941

# Clinical Notes

## CARDINAL POINTS IN THE STATIC AND IN THE DYNAMIC EYE

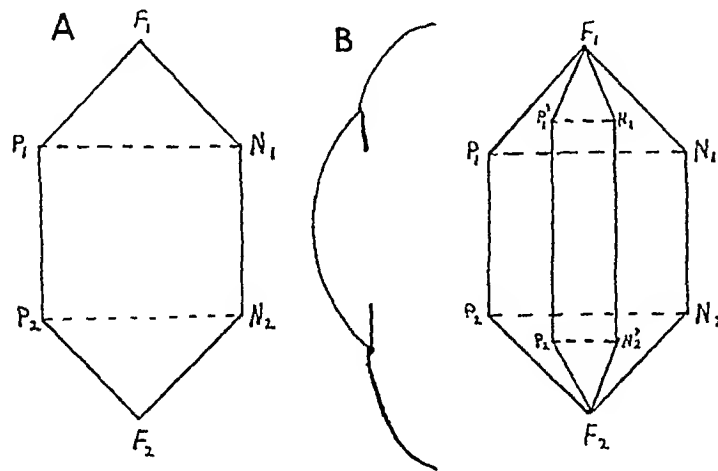
JOSEPH I PASCAL, M D, NEW YORK

The eye like every compound optical system, has six important reference points (and planes) —the so-called cardinal points. These are the two principal focal points, designated as  $F_1$  and  $F_2$ , the two principal points,  $P_1$  and  $P_2$ , and the two nodal points,  $N_1$  and  $N_2$ . Once these six points are located (in fact, even the first four suffice), calculations and constructions for image position, image magnification, etc., are easily made.

A scheme for remembering the relative distances between these cardinal points was previously published<sup>1</sup>. This method utilizes the

points resulting from accommodation can be visualized and easily remembered by utilizing another benzene ring inside the original ring. This is a thinner and longer "ring," placed as in figure, B. I shall designate the principal and the nodal points of the accommodated eye as  $P_1'$ ,  $P_2'$ ,  $N_1'$ ,  $N_2'$  (read P one prime, etc.)

It is known that since the accommodated eye is a stronger optical system, its focal distances must be shorter. A glance at the diagram (B) shows this, as  $F_1$  is closer to  $P_1'$  than it is to  $P_1$  and  $F_2$  is closer to  $P_2'$  than it is to  $P_2$ . The distance between any two points may be repre-



Scheme to show cardinal points (A) in the static (nonaccommodated) eye and (B) in the accommodated eye

well known benzene ring, on which the cardinal points are placed, as in A of the figure. Any two opposite sides which are parallel are equal. Thus if the distance between any two points is represented by the two corresponding letters,  $P_1 F_1 = N_2 F_2$ ,  $P_2 F_2 = N_1 F_1$ ,  $P_1 P_2 = N_1 N_2$ , and  $P_1 N_1 = P_2 N_2$ . The distance between the principal point and the corresponding nodal point, i.e.,  $P_1 N_1$  or  $P_2 N_2$ , is equal to the radius of the single refracting surface which can replace the whole ocular system. This potential radius is equal to the difference between the principal focal lengths.

Now, when the eye accommodates it becomes a different, specifically a stronger, optical system. This causes a displacement of all the cardinal points, so that they occupy different positions in the accommodated eye than they did in the nonaccommodated eye. The shift in the cardinal

points is represented by the two corresponding letters, and one sees that the distance between the principal points in the accommodated eye,  $P_1'$  and  $P_2'$ , has increased, as has the distance between the two nodal points,  $N_1'$  and  $N_2'$ . The distance between the principal and the corresponding nodal point has decreased. That is,  $P_1' P_2'$  is more than  $P_1 P_2$ ,  $N_1' N_2'$  is more than  $N_1 N_2$ ,  $P_1' N_1'$  is less than  $P_1 N_1$  and  $P_2' N_2'$  is less than  $P_2 N_2$ .

The equality of opposite parallel sides, of course, holds as good in the inner "ring" as in the outer "ring". Thus,  $P_1' F_1 = N_2' F_2$ ,  $P_2' F_1 = N_1' F_2$ , and so on.

As a result of the increase of power, one knows that  $F_1$  and  $F_2$  must have moved closer to the cornea. The diagram shows that as a result of the accommodation the two principal points have moved farther apart, as have the two nodal points. Also, the principal and the corresponding nodal point have moved closer together.

When one visualizes the cornea to the left of the "ring" in B, one sees what happens during

1 Pascal, J. I. A Memory Scheme for the Cardinal Points. Arch. Ophth. 22:448 (Sept.) 1939

accommodation The principal points have moved farther away from the cornea,  $P_1$  to  $P_1'$ , and  $P_2$  to  $P_2'$ , the nodal points have moved closer to the cornea,  $N_1$  to  $N_1'$  and  $N_2$  to  $N_2'$ . This movement of the principal and the nodal points brings the corresponding pairs closer together and shows the increased power of the system. For  $P_1 N_1$  in the nonaccommodated eye and  $P_1' N_1'$  in the accommodated eye, each represents the equivalent radius of curvature of a single refracting surface which could replace the whole optical system.

The forward movement of the nodal points explains why the retinal image, irrespective of its

clearness, is larger in the accommodated eye than it is in the nonaccommodated eye. The greater separation of the nodal points in the accommodated eye also shows that the displacement of the axial ray is greater in the accommodated eye than it is in the nonaccommodated eye.

Thus, the long benzene "ring" inside the regular "ring" shows at a glance the changes taking place in the position of the cardinal points when the eye accommodates and their significance. With the aid of the double "ring" these relationships can be easily remembered.

37 West Ninety-Seventh Street

# Ophthalmologic Reviews

EDITED BY DR FRANCIS HEED ADLER

## RETINAL VASCULAR MICROMETRY AND ESSENTIAL HYPERTENSION

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Variations in the diameters of retinal vessels observable ophthalmoscopically in the eyes of normal and of hypertensive persons have drawn the attention of numerous workers since the first report of retinitis in nephritis was published by von Graefe,<sup>1</sup> in 1855, however, Liebreich,<sup>2</sup> in 1859, in his detailed description of "albuminuric retinitis," was the first to mention the existence of narrowed arterial vessels

Frequent attempts have been made since the initial published method by Ruete,<sup>3</sup> in 1852, to obtain absolute measurements of the delineable ophthalmoscopically visible retinal structures in the living human eye (table 1) The basic goal has been the attainment of unquestionable accuracy by practical means Numerous ingenious instruments and methods have been devised, all of which, however, in some manner combine a grid, graticule or micrometer scale with an ophthalmoscopic apparatus The application of retinal photography, as advocated by Tengroth<sup>4</sup> and by Nordenson,<sup>5</sup> provides for the later, and more leisurely, analysis of structures that previously had undergone examination Haessler and Squier<sup>6</sup> employed this method in 1931 in their study of the alterations in caliber of the retinal arterioles in persons with early hypertension Puntenney,<sup>7</sup> more recently, has employed

experimentally the method suggested by Lambert,<sup>8</sup> in 1934, by means of which direct microscopic examination of the living eye is facilitated by the use of a planoconcave contact glass A miniature camera and a micrometer ocular attachment were used to provide photographic records of intraocular vessels under varying pharmacologic changes of environment

The earliest investigators devised crude grids or graticules for use with reflecting mirrors and indirect ophthalmoscopy, but it was not until 1864 that the first measurements of the caliber of the arterial vessels of the human retina were published by Zander<sup>9</sup> (table 2) Subsequent technical improvements in the construction of ophthalmoscopes and their accessories made possible the eventual incorporation of the Morgan<sup>10</sup> graticule in the Keeler hand instrument for direct ophthalmoscopy This graticule, or some modification of it, is the most readily utilizable hand grid measuring method now currently in use, its convenience obviates the necessity of transporting the patient to a more complicated, stationary apparatus

In my own studies a modified Morgan graticule incorporated in a Keeler ophthalmoscope was used<sup>11</sup> This instrument previously had been employed by Wagener<sup>12</sup> (1931) and by Cusick and Herrel<sup>13</sup> (1939) in their investigations

From the Departments of Ophthalmology of Bellevue Hospital and New York University, and the Manhattan Eye, Ear and Throat Hospital

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TABLE 1—*Micrometry of Intraocular Structures Chronologic Development*

Year	Author	Measuring Device Employed	Unit Taken as Constant
1852	Ruete <sup>3</sup>	Graticule, indirect ophthalmoscopy	
1854 55	Ruete, C G T Lehrbuch der Ophthalmologie, ed 2, Braunschweig, Friedrich Vieweg u Sohn, 1855, vol 1	Graticule, indirect ophthalmoscopy	
1854	Donders, F C Arch f Ophth 1 (pt 2) 75-105, 1854 1855	Approximating pointers, micrometer scale, indirect ophthalmoscopy	
1857	Schneller, J J M Arch f Ophth 3 (pt 2) 120-186, 1857	Approximating pointers linear measurements, indirect ophthalmoscopy	
1878	Landolt, L Mikrometrie des Augengrundes, in Graefe, A, and Saemisch, T Handbuch der gesamten Augenheilkunde, ed 2, Leipzig, Wilhelm Engelmann, 1904, vol 4, pt 1, pp 48-51	Graticule, indirect ophthalmoscopy, formulas	Disk = 1.5 mm
1907	Fortin, E P Arch d'opht 27 397-405 (June) 1907	Entoptoscopy	
1922	Lo Cascio <sup>10</sup>	Graticule, heliometer	
1924	Henriksson <sup>17</sup>	Split prism ocular	
1926	Bretagne, M P Ann d'oeu 163 192-198, 1926	Graticule, formulas	
1926	Dufour, M Ann d'oeu 163 193-201, 1926	Graticule, formulas	
1930	Tengroth <sup>4</sup>	Retinal photography, micrometer scale, microcomparator	Structures measured in 0.01 disk diameter
1930	Margotta, G Ann di ottal e clin ocul 58 676-700 (Aug Sept) 1930	Graticule, formulas	Disk value fixed
1931	Nordenson <sup>5</sup>	Retinal photography, stereo micrometer scale	Structures measured in 0.01 disk diameter
1931	Haessler and Squier <sup>6</sup>	Retinal photography, Gaertner comparimeter microscope	
1932	Lambert, R K Arch Ophth 7 440-443 (March) 1932	Ophthalmoscope grid	
1934	Spinelli, F Klin Monatsbl f Augenh 92 93-107 (Jan) 1934	Modified perimeter, micrometer or graticule scale	Disk value fixed
1934	Lambert <sup>8a</sup>	Retinal photography, contact glass, micrometer scale	
1935	Lambert <sup>8b</sup>	Retinal photography, contact glass, micrometer scale	
1939	Puntenney <sup>7</sup>	Lambert method	
1940	Cotton, Lewis and Egenhofer <sup>23</sup>	Lobeck method, corrected formulas	Disk = 1.43 mm
1940	Cotton and Rosin <sup>24</sup>	Lobeck method, corrected formulas	

TABLE 2—*Caliber of Normal Retinal Arterioles*

Year	Author	Measuring Device Employed	Unit Taken as a Constant	Point at Which Measurements Were Made	Caliber of Arterioles, Mm		
					Nasal	Temporal	All Vessels
1864	Zander <sup>9</sup>	Graticule					0.064 to 0.118
1907	Dimmer, F Klin Monatsbl f Augenh 45 296-329, 1907	Graticule, photography	Known diameter of papilla	At disk margin			0.093
1919	Hess, C Arch f Augenh 54 110, 1919	Graticule	Disk = 1.5 mm	At disk margin			0.100
1926	Lo Cascio <sup>18</sup>	Graticule, heliometer principle	Disk = 1.5 mm	At disk margin			0.110 to 0.120
1931	Wagener <sup>12</sup>	Morgan graticule, Keeler ophthalmoscope		½ disk diameter from disk margin	0.050 to 0.060	0.100 to 0.060	
1934	Lobeck <sup>19</sup>	Gullstrand ophthalmoscope, Lobeck heliometer	Disk = 1.5 mm	At disk margin			0.140 to 0.150
1936	Neame <sup>14</sup>	Morgan graticule, Keeler ophthalmoscope	Disk = 1.5 mm	At disk margin			0.086 to 0.094
1937	Lobeck <sup>20</sup>	Gullstrand ophthalmoscope, Lobeck heliometer	Disk = 1.5 mm	At disk margin			0.088 to 0.134
1937	Kuhn <sup>21</sup>	Lobeck's method	Disk = 1.5, 1.6 and 1.7 mm	At disk margin			0.086 to 0.138
1937	Badtke <sup>22</sup>	Lobeck's method	Disk = 1.5 mm	At disk margin		0.090 to 0.112	
1939	Rucker <sup>25a</sup>	Prism displacement method	Assumes nodal point of 17 mm	½ disk diameter from disk margin			0.070 to 0.140
1939	Cusick and Herrel <sup>13</sup>	Morgan graticule, Keeler ophthalmoscope		½ disk diameter from disk margin	0.050 to 0.060	0.100 to 0.120	
1940	Cusick, Benson and Boothby <sup>25b</sup>	Morgan graticule, Keeler ophthalmoscope, Rucker prism displacement method		½ disk diameter from disk margin			0.072 to 0.102
1941	Koch <sup>11</sup>	Morgan graticule, Keeler ophthalmoscope		1 disk diameter from disk margin	0.047 to 0.124	0.062 to 0.140	0.047 to 0.140

The graticule is cross lined into millimeter squares, and equidistant cross lines subdivide these into squares of 0.2 mm each. These individual squares, when focused on the retina in cases of emmetropia, bound an anatomic retinal surface area which has been calculated by the maker to measure 0.186 mm on each of its four inner margins. On ophthalmoscopic examination, the size of these smaller squares increases in cases of hyperopia, when projected on to the retina, and decreases in cases of myopia, for example, any side of such a square is equal to an anatomic distance of 0.190 mm at +3 D but only to 0.180 mm at -3 D.

The graticule is interposed in the beam emanating from the electric ophthalmoscope lamp and is focused sharply on the retina by adjustment of a separate attachment on the instrument. The

nally devised by Morgan in that squares and guiding lines of various sizes permit of a more versatile use. Another modification, introduced by the maker in the more recent "Decagon" model, has been studied by Berens and McLaughlin.<sup>15</sup> The value for each smaller square in this instrument in the emmetropic eye is equal to 0.1408 mm, also, there is a larger central square in which lines of varying thickness have been etched, so that retinal structures as small as one third of a square may be measured. It is thought that errors of measurement dependent on estimation of size are decreased by the use of this innovation, however, there is as yet no confirmation of this statement.

Wagener,<sup>12</sup> in 1931, in measuring the retinal arterioles before and after cervicothoracic sympathetic ganglionectomy, and Cusick and Herrel,

TABLE 3—Table of Equivalents for Modified Morgan Graticule in Keeler Ophthalmoscope

Dioptric Strengths	Value of Graticule Squares in Mm	Fractional Estimation of Squares and Corrected Values in Microns					
		$\frac{1}{8}$	$\frac{1}{4}$	$\frac{3}{8}$	$\frac{1}{2}$	$\frac{5}{8}$	$\frac{3}{4}$
+10.00	0.192	38.40	48.00	64.00	96.00	128.00	144.00
+8.00	0.1916	38.32	47.90	63.87	95.80	127.73	143.70
+6.00	0.1913	38.26	47.83	63.77	95.65	127.53	143.48
+4.00	0.191	38.20	47.75	63.66	95.50	127.33	143.25
+3.00	0.190	38.00	47.50	63.33	95.00	126.66	142.50
+2.00	0.189	37.80	47.25	63.00	94.50	126.00	141.75
+1.00	0.188	37.60	47.00	62.66	94.00	125.32	141.00
0.00	0.186	37.10	46.50	62.00	93.00	124.00	139.50
-1.00	0.184	36.80	46.00	61.33	92.00	122.66	138.00
-2.00	0.182	36.40	45.50	60.66	91.00	121.32	136.50
-3.00	0.180	36.00	45.00	60.00	90.00	120.00	135.00
-4.00	0.178	35.60	44.50	59.33	89.00	118.66	133.50
-6.00	0.172	34.40	43.00	57.33	86.00	114.66	129.00
-8.00	0.164	32.80	41.00	54.66	82.00	109.32	123.00
-10.00	0.150	30.00	37.50	50.00	75.00	100.00	112.50

spherical refractive power of the eye under examination is indicated as in other standard ophthalmoscopes. The maker has furnished a correction table for the various dioptric strengths necessarily employed in bringing into clear view the intraocular structures being measured. These strengths range from +10 D through 0 to -10 D, inclusive. Since retinal vessels occupy only a portion of any small square of the graticule projected on the retina, fractional estimation of their relative size must be made. A monogrammic table of equivalents was devised to facilitate the conversion of these values to microns (table 3).

The instrument employed by Neame<sup>14</sup> (1936) was the Keeler ophthalmoscope in which he had incorporated his modification of the Morgan graticule. The graticule differs from that origi-

nally devised by Morgan in that squares and guiding lines of various sizes permit of a more versatile use. Another modification, introduced by the maker in the more recent "Decagon" model, has been studied by Berens and McLaughlin.<sup>15</sup> The value for each smaller square in this instrument in the emmetropic eye is equal to 0.1408 mm, also, there is a larger central square in which lines of varying thickness have been etched, so that retinal structures as small as one third of a square may be measured. It is thought that errors of measurement dependent on estimation of size are decreased by the use of this innovation, however, there is as yet no confirmation of this statement.

Lo Cascio,<sup>16</sup> in 1922, appears to have devised a formula based on principles employed in

15 Berens, C, and McLaughlin, C K. The Keeler Decagon Ophthalmoscope as a Refractometer, *Am J Ophth* 17 402-416 (May) 1934.

16 Lo Cascio, G. Un nuovo metodo per la determinazione della grandezza reale di tratti di fondo oculare a mezzo dell'oftalmoscopio, *Riv d'ottica* 2 51-64 (July) 1922.

14 Neame, H. A Method of Estimating the Calibre of Retinal Arteries in the Living Eye by Means of the Ophthalmoscope, Illustrated by Results in Some Normal and Pathological Cases. *Tr Ophth Soc U Kingdom* 56 155-162, 1936.

astronomy, which, when applied to observation of the retinal structures with Gullstrand and Thorner ophthalmoscopes, anticipated the later work of Henriksson<sup>17</sup> Lo Cascio,<sup>18</sup> in 1926, published a few measurements of the caliber of retinal arterial vessels at the margin of the disk in a small group of persons, of whom some were normal adults and some had chronic renal disease

Lobeck,<sup>19</sup> in 1934, described his method and apparatus for the measurement of ophthalmoscopically visible retinal structures. The device is based on the principles of heliometry and is installed in the reflex-free, simplified Gullstrand ophthalmoscope. Henriksson,<sup>17</sup> in 1924, had suggested their application, but, unlike the modification offered by Lobeck,<sup>19</sup> Henriksson's instrument was so constructed that the lens of the objective was split, while in Lobeck's the ocular was split. The earlier work of Lo Cascio<sup>18</sup> appears to have been unknown to these two authors.

It is possible with his apparatus, according to Lobeck,<sup>20</sup> writing in 1934 and in 1937, to measure the optic papilla with absolute accuracy and, by splitting the ocular and making positional adjustments of its axis, to determine the diameter of the retinal vessels at any point on the disk or at its margin by a direct reading from the scale mounted on the ocular which Nonius incorporated in the apparatus. It is necessary, however, to accept as a constant unit the figure of 1.5 mm as representing the horizontal diameter of the disk. Lobeck cited several authors to support his contention that this is the mean anatomic size of the nerve head.

Kuhn,<sup>21</sup> in 1937, employed the Lobeck heliometer and measured the papillas and the retinal vessels at the margins of the disks of 100 normal adults. He assumed arbitrary successive papilla diameters of 1.5, 1.6 and 1.7 mm in order to compare the probable accuracy of the measurements he made of the retinal vessels. He calculated first the true values of the measured relative values, working from a basic absolute hori-

zontal diameter of the papilla of 1.5 mm, as did Lobeck. His conclusions tended to confirm the results of the latter, and he came to the conclusion that in normal adults retinal arteries that measured less than 86 microns or more than 138 microns in caliber at the rim of the papilla and retinal veins that measured less than 100 microns or more than 159 microns at the same location were narrower and wider, respectively, than normal.

Badtke,<sup>22</sup> in 1937, also using the Lobeck apparatus, obtained essentially the same range of measurements of retinal arterial vessels in normal persons. Cotton, Lewis and Egenhofer,<sup>23</sup> however, in 1940, employed a modification of the method of calculation described by Lobeck in that they applied a factor for the refractive correction of each eye of their subjects to a formula from which they believed that the exact magnification of retinal structures observed with the Lobeck device could be determined. They expressed the opinion that the mean figure of 1.5 mm for the horizontal diameter of the disk, as proposed by Lobeck and accepted by Kuhn and by Badtke, permitted too large an error, since they found in a small group of cases that the true disk diameter varied from 1.2 to 1.7 mm. The mean value obtained was 1.43 mm.

These authors stated the belief, also, that it was necessary to measure the diameter of each retinal vessel rather than only one or a few of them because an additional factor of error would be introduced if this were not done. They gave no figures, however, for the diameters of the vessels measured but calculated in square millimeters the entire retinal vascular bed at the margin of the disk by measuring the caliber of all the vessels, both arterial and venous, in each eye at that location. These figures, they stated, were free from any assumed values.

They concluded that the total retinal vascular bed probably was diminished in certain deteriorative mental diseases. It should be pointed out, however, that Kuhn found smaller vascular diameters when correcting his figures on the basis of a papilla diameter of 1.6 mm than when he used larger disk sizes. In the absence of recorded actual values for vascular diameters, it is reasonable to suppose that had Cotton, Lewis and Egenhofer given these figures, they would have

17 Henriksson, V. *Oftalmomikrometriska försök*, Hygiea **86** 887, 1924.

18 Lo Cascio, G. *Ricerche cliniche, anatomo-patologiche e patogenetiche sulla neuroretinite nefritica*, Ann di ottal e clin ocul **54** 3-64 (Jan) 1926.

19 Lobeck, E. *Ueber Messungen am Augenhintergrunde*, Arch f Ophth **133** 152-165 (Nov) 1934.

20 Lobeck, E. (a) *Ueber den Durchmesser der Netzhautgefäße am gesunden und kranken Menschen*, Arch f Ophth **136** 439-456 (Feb) 1937, (b) footnote 19.

21 Kuhn, W. *Ueber Messungen am Augenhintergrunde*, Arch f Ophth **138** 129-148 (Oct) 1937.

22 Badtke, G. *Kalibermessungen an den Netzhautgefäßen bei Hochdruck- und Nierenkranken*, Klin Monatsbl f Augenh **99** 655-669 (Dec) 1937.

23 Cotton, J. M., Lewis, N. D. C., and Egenhofer, A. W. *Vascular Bed of the Retina in Mental Disease*, Arch Neurol & Psychiat. **43** 891-900 (May) 1940.

been smaller generally than those of Kuhn, since these three co-authors in their study determined the anatomic value of the disk to be 1.43 mm. Cotton and Rosin<sup>24</sup> further refined the formula method and concluded that measurements thus obtained probably were reliable to 0.01 mm.

There should be mentioned here the prism displacement method of Rucker<sup>25</sup> (1939), which assumes a nodal point of approximately 17 mm and, therefore, a lesser magnification of the fundus than that of 14 to 15 diameters which is believed to be obtained with the standard hand ophthalmoscope.<sup>26</sup> His values for the caliber of the arterial vessels of the human retina compare favorably with those obtained by other workers with other methods.

It is difficult, however, to compare the figures obtained by the various investigators, since dissimilar instruments have been employed, methods and subjects have varied greatly and the sites at which the vessels were measured also have been unlike. Certain of the workers measured only some, or not all, of the vessels. All the figures obtained undoubtedly reflect to some degree the intangible factor inherent in the clinical fact that not only the observer but the subject was not a precision machine. Therefore, no matter how carefully and patiently the measurements were made, some deviations from absolute accuracy probably have occurred. Thus, it would appear that the recorded measurements of the diameters of retinal vessels in the living eye probably should be considered in the main as no more than approximately or reasonably accurate.

A comparison of the average or ranges of the figures for all arterial vessels, whether measured with the graticule instruments or with the heliometer devices, reveals no notable discrepancy if it is recalled that the use of the latter necessitates the measurement of the vessels at the margin of the papilla, where the diameters are readily seen to be greater than when observed more peripherally. Thus, all of the retinal arterial vessels in the vicinity of the nerve head in normal persons, with no systemic or local vascular dis-

ease, are found to range in caliber, as determined from all available published figures, from 50 to 120 microns when measured with the graticule and from 86 to 150 microns when measured with the heliometer (table 2).

#### ANATOMY AND PHYSIOLOGY OF THE ARTERIAL VESSELS OF THE RETINA

The ophthalmic artery in man branches directly from the internal carotid artery and is considered by some authorities virtually a branch of the circle of Willis. The internal carotid artery narrows immediately after it gives off the ophthalmic artery. The latter averages 1.5 mm in diameter while the former averages 5.4 mm in diameter just proximal to the branching off of the ophthalmic artery and 3.8 mm just distal to that point. A high pressure in the ophthalmic artery is believed to be maintained by this reduction in caliber of the internal carotid artery.<sup>27</sup>

The central artery of the retina arises from the ophthalmic artery on the entrance of the latter into the orbit. The former then traverses the lateral surface of the optic nerve until it enters the nerve, usually at a distance of 10 to 15 mm. posterior to the globe. The artery bifurcates within the intraocular portion of the optic nerve into a superior and an inferior papillary artery. Ophthalmoscopically, these two branches are not always fully visible because they exhibit remarkable variability in their anatomic lengths and in their points of emergence on to the papilla, however, they rarely extend beyond the rim of the optic disk. Each of these two arteries divide, in turn, to give rise normally to temporal and nasal arterial branches, which traverse the nerve fiber layer of the retina and supply the retinal quadrants to their peripheries.

Friedenwald,<sup>28</sup> in considering the role of arterial vessels of the retina, stated "It is of no interest whether these vessels are arteries or arterioles." Wagener<sup>29</sup> pointed out, however

Perhaps of first importance in the interpretative study of the retinal arterial vessels is the decision as to whether they should be regarded as arteries or arterioles.

The central artery of the retina does not differ

24 Cotton, J. M., and Rosin, S. Measurement of the Structures of the Fundus, *Arch Ophth* **23** 1146-1156 (June) 1940.

25 (a) Rucker, C. W. Personal communication to the author, 1939. (b) Casick, P. L., Benson, O. O., Jr., and Boothby, W. M. Effect of Anoxia and of High Concentrations of Oxygen on the Retinal Vessels. Preliminary Report, *Proc Staff Meet, Mayo Clin* **15** 500-502 (Aug 7) 1940.

26 Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company 1933, vol 1

27 Whitnall, S. E. *The Anatomy of the Human Orbit and Accessory Organs of Vision*, ed 2, London, Oxford University Press, 1932. Friedenwald, J. S.: *Retinal Vascular Dynamics*, *Am J Ophth* **17** 387-395 (May) 1934.

28 Friedenwald, J. S. The Pathology of the Ocular Changes in Nephritis and Hypertension, in Berglund, H., and Medes, G. *The Kidney in Health and Disease*, Philadelphia, Lea & Febiger, 1935, pp 638-664.

29 Wagener, H. P. The Nature and Significance of the Retinal Lesions Associated with Hypertensive Disease, *Tr Am Acad Ophth* **44** 54-74, 1939.

essentially from other vessels of similar size in its course through the orbit and the optic nerve, however, after the artery passes through the lamina cribosa of the optic nerve, the arterial coat diminishes rather abruptly to about one third of its previous thickness. This transition normally is less obvious between the central artery and the papillary arteries than it is between the latter and the retinal arterial vessels proper. These smaller vessels diminish progressively in caliber to capillary size.

Friedenwald<sup>28</sup> has observed that the reduction in caliber is due largely to the diminution of the media, although the adventitia becomes thinner and looser in structure. The histologic demonstration of the presence of smooth muscle fibers in the normal retinal arterial branches is difficult, but the presence of contractile elements on both clinical and experimental grounds is conceded by this worker. The elastic lamella at first is preserved but becomes somewhat reduced in density until it no longer can be seen in the more distal secondary branches and in the tertiary branches. The intima remains unchanged. The veins and the arteriolar and venous capillaries normally are differentiated histologically from precapillary arterial vessels of any size by their lack of smooth muscle cells and the presence of an internal elastic lamella.

The retinal vessels sustain an internal pressure approximately equal to that sustained by vessels of a similar order of size elsewhere in the body, but the pressure in the terminal arterioles most probably is somewhat higher than the average elsewhere. The intraocular pressure of some 20 mm of mercury, however, exerts an external supportive force on the intraocular vessels. Friedenwald<sup>28</sup> stated

It is perhaps as a response to this relief from internal strain that the unusual delicacy of the retinal arterial wall is to be understood. This delicacy of structure may explain the unusually great local effects of changes in blood pressure if these local effects are truly disproportionate to those in other organs and not merely more easily recognizable.

He also suggested that relative malnutrition of the walls of the retinal arterial vessels may result in fibrous thickening of the media and adventitia since there exist no vasa vasorum in these small vascular channels.

The size of the arterial vessels in the retina, as well as those of similar caliber elsewhere in the body, has interested many observers. Kernohan, Anderson and Keith<sup>30</sup> and their co-workers

classified small arterial vessels of diameters ranging from 25 to 125 microns as arterioles. Others have placed the upper limit of arteriolar diameters at 150 microns, while Bell<sup>31</sup> stated his opinion that this limit should not exceed 40 microns. The muscle and the internal elastic lamina, however, already have been reduced to a minimum in vessels of the latter caliber, and such vessels should be considered precapillary arterioles.

These workers studied fixed tissues stained with standard or special dyes and examined microscopically. Only vessels that were cut to true cross sections were measured. A monocular micrometer for incorporation in a standard microscope was used. The distinction between arteries and arterioles in their studies, therefore, is largely an arbitrary one and is based on the diameter of the vessel rather than on other criteria, since there exists no true anatomic distinction, such as that between the structure of venous and of arterial vessels of precapillary size or larger.

Ophthalmoscopically, measurements of the retinal arterial vessels, whether made with the gaticule or with the heliometer, have been taken in the main at the margin of the optic disk. The previous exceptions have been those made by Wagener<sup>12</sup> and by Cusick and Herrel<sup>13</sup>. These workers have referred to the retinal arterial channels measured by them as arterioles, the other investigators have termed these vessels arteries although their recorded measurements of these vessels at the margin of the papilla, or just immediately peripheral to that point, in the living human eye do not exceed the arbitrary upper limit set for arteriolar caliber. Inadvertently, the papillary arteries occasionally may have been measured.

It would appear, then, that the retinal branches of the central artery of the retina should be designated as arterioles, since they are within the limits of size of arterioles in general. Wagener<sup>29</sup> pointed out that this is of clinical importance when he stated, "Lesions observed in the retinal arterial vessels should be considered as indicative of systemic arteriolosclerosis, rather than of arteriosclerosis."

#### COMMENT

Wagener and Keith,<sup>32</sup> in their recent review of diffuse arteriolar disease with hypertension and the associated retinal lesions, stated "Any elevation of systemic blood pressure is probably

31 Bell, E. T., cited by Wagener<sup>29</sup>

30 Kernohan, J. W., Anderson, E. W., and Keith, N. M. The Arterioles in Cases of Hypertension, *Arch. Int. Med.* 44:395-423 (Sept.) 1929.

32 Wagener, H. P., and Keith, N. M. Diffuse Arteriolar Disease with Hypertension and the Associated Retinal Lesions, *Medicine* 18:317-430 (Sept.) 1939.

accompanied by a rise of blood pressure in the retinal arterial system" Baillart<sup>33</sup> and his followers and Saganuma and others<sup>34</sup> have demonstrated that the rise in the retinal intra-arterial pressure under varying conditions may or may not be proportional to the elevation of pressure in the brachial arteries. The coincidental and associated changes, both physiologic and structural, that occur in the retina and in its vessels with elevation of the systemic and, presumably then, of the retinal blood pressure lend themselves to early recognition by the usual ophthalmoscopic methods, and information of considerable clinical value may be obtained by careful examination. This interpretative procedure is valuable in differentiating the various types of systemic vascular disease in which elevations of blood pressure occur. Wagener and Keith<sup>32</sup> stated

If it can be assumed, as seems logical, that the visible reactions in the retinal vessels are similar, though at times disproportionate, to the invisible reactions taking place in vessels of similar size throughout the body, it is obvious that an explanation of the mechanism of these reactions in the retina will go far toward solving the mechanism of diffuse vascular disease. This phase of ophthalmoscopy is of particular interest to the internist.

It is now generally accepted that widespread increased peripheral resistance to blood flow in hypertensive, vascular renal disease results in an elevation of systemic blood pressure and that

33 Baillart, P. *Circulation arterielle rétinienne. Essais de détermination de la tension artérielle dans les branches de l'artère centrale de la rétine*, Ann d'ocul **154**:257-271, 1917, *La pression artérielle dans les branches de l'artère centrale de la rétine. Nouvelle technique pour la déterminer*, ibid **154**:648-666, 1917, *La circulation rétinienne à l'état normal et à l'état pathologique. Procédés modernes d'examen et de diagnostic*, Paris, Gaston Doin, 1923, *The Retinal Circulation in the Normal and Pathologic State*, translated by J. E. Lebensohn, Chicago, The Professional Press Inc., 1928, *Quelques considérations sur la pression dans la veine centrale de la rétine*, Ann d'ocul **168**:513-539 (July) 1931, *L'hypertension artérielle rétinienne*, Tr. Internat. Cong. Ophth. (1937) **1**:87-142, 1938, Baillart, P., Magniel, and Saragea. *Mesures de la pression artérielle rétinienne et de la tension céphalo-rachidienne dans quelques cas d'hypertension artérielle*, Arch. d'mal. du cœur **17**:289-294 (May) 1924.

34 Saganuma, S. *Studien über den Blutdruck in der Zentralarterie der Netzhaut. I. Ueber den Blutdruck in der Zentralarterie der Netzhaut bei gesunden Menschen und über seine Beziehung zum allgemeinen Blutdruck*, Klin. Monatsbl. f. Augenh. **96**:74-84 (Jan) 1936, *II. Ueber den Blutdruck in der Zentralarterie der Netzhaut bei verschiedenen Formen von allgemeiner Hypertonie und über die sog. isolierte zephalische Hypertension*, ibid **97**:498-514 (Oct) 1936, *III. Ueber den Blutdruck in der Netzhautarterie während des Verlaufes der normalen Schwangerschaft und der Schwangerschaftstoxikose, sowie über seine frühdiagnostische Bedeutung*, ibid **99**:637-654 (Nov) 1937. Koch<sup>11</sup>

the arterioles, in the main, are the seat of this increased resistance. Richard Bright,<sup>35</sup> in 1836, in speculating on the cause of cardiac hypertrophy associated with renal disease, suggested that the two most logical explanations for the apparently increased work that the heart had performed were "either that the altered quality of the blood affords unwonted stimulus to that organ immediately, or that it so affects the minute and capillary circulation as to render greater action necessary to force the blood through the distant subdivisions of the vascular system."

One of the first to suggest that there was present a vascular factor in addition to the renal lesion in Bright's disease was Johnson,<sup>36</sup> in 1868. He stated

In every fatal case of chronic Bright's disease with hypertrophy of the left ventricle there has been decided hypertrophy of the arterial walls in most of the tissues examined, not only in the kidneys, but also in the skin, the intestines, the muscles, and the pia mater. The facts hitherto observed all point to the conclusion that hypertrophy of the walls of the small arteries is a result of their continued overaction in opposition to the heart.

Johnson, however, as did Bright, believed that the primary disease is in the kidney.

Gull and Sutton<sup>37</sup> in 1872, stated the opinion that the pathologic lesions observed at autopsy in the heart and in the kidney in cases of chronic Bright's disease are secondary to primary disease of the peripheral capillaries and arterioles. There still is no unanimity, according to Keith,<sup>38</sup> concerning which of these two points of view approaches the truth.

Mahomed,<sup>39</sup> in 1879, expressed the opinion that high arterial pressure could exist in adults who were less than 30 years of age and did not exhibit any other physical signs of disease and/or structural changes in the vessels. He termed this condition the "pre-albuminuric stage" of Bright's

35 Bright, R. *Cases and Observations Illustrative of Renal Disease Accompanied with the Secretion of Albuminous Urine*, Guy's Hosp. Rep. **1**:338-379, 1836, *Tabular View of the Morbid Appearances in One Hundred Cases Connected with Albuminous Urine*, ibid **1**:380-400, 1836.

36 Johnson, G. I. *On Certain Points in the Anatomy and Pathology of Bright's Disease of the Kidney*, II. *On the Influence of the Minute Blood-Vessels upon the Circulation*, Med.-Chir. Tr. **51**:76, 1868.

37 Gull, W. W., and Sutton, H. G. *On the Pathology of the Morbid State Commonly Called Chronic Bright's Disease with Contracted Kidney*, Med.-Chir. Tr. **55**:273-326, 1872.

38 Keith, N. M. *General Consideration of the Relationship of Hypertension to Renal Disease*, Proc. Staff Meet., Mayo Clin. **15**:465-467 (July 24) 1940.

39 Mahomed, F. A. *Some of the Clinical Aspects of Chronic Bright's Disease*, Guy's Hosp. Rep. **24**:363-426, 1879.



disease because he felt that these persons would have chronic Bright's disease sooner or later. In 1893 von Basch<sup>40</sup> stated "There are numerous cases in which examination reveals a high tension of the pulse but the older characteristics of outspoken arteriosclerosis are either absent or minimal." He termed this condition "latent arteriosclerosis." A similar entity was represented by Huchard's<sup>41</sup> "presclerosis," described in 1899.

A modified point of view was advanced by Jores<sup>42</sup> in 1904, who expressed the opinion that the vascular changes in the small arteries that he observed in varying degrees in the viscera in cases of nephritis, but never in the heart and the skeletal muscles, resulted, when present, in materially influencing the progress and outcome of the disease.

The term "hyperpiesia" was introduced by Clifford Allbutt,<sup>43</sup> to whom Wagener and Keith<sup>32</sup> have stated should go "perhaps the greatest credit for the recognition of the syndrome of essential hypertension." Hyperpiesia, atherosclerosis and chronic nephritis were well established entities in 1915, when Allbutt's book, "Diseases of the Arteries, Including Angina Pectoris," was published.

It was Janeway,<sup>44</sup> in 1913, who, in reviewing and summarizing to date the then existing knowledge of cardiovascular-renal disease, spoke of alterations in the vasomotor regulation of the small arterial vessels in essential hypertension, stating

The renal disease back of what we call chronic interstitial nephritis is a disease of the small blood vessels and the lesions of the kidney are secondary manifestations.

From the standpoint of physiology the high blood pressure is the evidence of arteriolar disease rather than renal. It must be interpreted as a sign of abnormal irritability of the constrictor mechanism. Disturbed vasomotor regulation not permanent obliteration is the usual important factor.

And, in writing of hypertension subsequent to renal disease, he added that hypertension also may develop "in primary irritability of the vasoconstricting mechanism from unknown, probably

external causes, which lead eventually to arteriolar sclerosis."<sup>44</sup>

The investigations of Volhard,<sup>45</sup> whose contributions with regard to bilateral hematogenous renal disease were reviewed recently by Wagener and Keith,<sup>32</sup> probably have been the most valuable of recent years. Volhard seems to have been the first<sup>46</sup> (1918) to direct attention to the significance of angiospasm of the arterioles in hypertensive disease. The presence of arterial constriction or hypertonus, however, already had been suspected or recognized, as has previously been noted. Thiel,<sup>47</sup> in the main, expressed agreement with the views of Volhard and accepted the results of Badtke with regard to diameters of retinal vessels in normal and in hypertensive patients. He expressed the opinion that the really alarming sign in cases of pale hypertension is the appearance or onset of angiospasm.

Both Volhard<sup>46</sup> and Goldblatt and his co-workers<sup>48</sup> stated the opinion that the direct action of a vasopressor substance on the walls of the arterioles produces contraction of those vessels. This assumption that prolonged spasm of the arteries or arterioles plays a role in the pathogenesis of hypertension has given rise to considerable discussion. The organic changes in the retinal arterioles subsequent to angiospastic activity in hypertensive disease and in nephritis appear to be more logically explained by Volhard's conception of angiospasm than by any other theory advanced. Wagener<sup>49</sup> reviewed the factors involved in the significance and production of spasm in retinal arteriolar disease and

45 Volhard, F. Elevated Blood Pressure, in Berglund, H., and Medes, G. The Kidney in Health and Disease, Philadelphia, Lea & Febiger, 1935, pp. 386-416.

46 Volhard, F. Die doppelseitigen hamatogenen Nierenerkrankungen (Bright'sche Krankheit), Berlin, Julius Springer, 1918.

47 Thiel, R. Die Bedeutung der Augenuntersuchung für die Diagnose und Differentialdiagnose der Hochdruck- und Nierenkrankheiten, Tr. Internat. Cong. Ophth. (1937) 2: 201-209, 1938.

48 Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W. Studies on Experimental Hypertension. I. The Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, J. Exper. Med. 59: 347-379 (March) 1934. Goldblatt, H. The Pathogenesis of Experimental Hypertension Produced by Renal Ischemia, J. A. M. A. 108: 675 (Feb. 20) 1937.

49 Wagener, H. P. (a) The Significance of Spasm in Retinal Arteriolar Disease and in Retinitis, Tr. Pacific Coast Oto-Ophth. Soc. 24: 165-177, 1939, (b) Retinal Lesions in Nephritis and Hypertension, in Berglund, H., and Medes, G. The Kidney in Health and Disease, Philadelphia, Lea & Febiger, 1935, pp. 622-631, (c) footnote 29.

40 von Basch, S. S. K. Allgemeine Physiologie und Pathologie des Kreislaufs, Vienna, A. Holder, 1892.

41 Huchard, H. Traite clinique des maladies du cœur et de l'aorte, ed. 3, Paris, O. Doin, 1899, vol. 3.

42 Jores, L. Ueber die Arteriosklerose der kleinen Organarterien und ihre Beziehungen zur Nephritis, Virchows Arch. f. path. Anat. 178: 376-406 (Dec.) 1904.

43 Allbutt, T. C. Senile Plethora or High Arterial Pressure in Elderly Persons, Tr. Hunterian Soc., 1896, pp. 38-57.

44 Janeway, T. C. Nephritic Hypertension. Clinical and Experimental Studies, Am. J. M. Sc. 145: 625-656 (May) 1913.

in retinitis and considered the theories advanced in explanation of Volhard,<sup>45</sup> Mylius,<sup>50</sup> Friedenwald,<sup>28</sup> Koyanagi,<sup>51</sup> Fritz,<sup>52</sup> Pal<sup>53</sup> and others

Pal's interpretation of the nature of arterial narrowing denies the possibility of the existence of continuous spasm, since it is not in accord with biologic experience with smooth muscle and with histologic investigations. Spasm, while a normal physiologic function in lower animal forms, also serves useful purposes in the higher animals. It frequently, however, is an untoward phenomenon in civilized man, particularly when the external environment becomes unduly competitive. It might be assumed that spasm as a protective function in urban man, therefore, often is harmful when it occurs as a physiologic response to stimuli originating in his now less dangerous environment. This response then becomes at first, certainly, one that is physiologic, but abnormally so, to the point where it might be considered psychopathophysiologic. Pal, who was one of the chief exponents of the existence of arteriolar spasm, stated the belief that the generalized arteriolar narrowing thought to be present with pathologic elevations of systemic blood pressure is due to continuous hypertonicity and not to active vascular spasm as such.

The resistance to the flow of blood in the arterioles is dependent on three factors: the viscosity of the blood, the velocity of the stream and the size of the lumen. The velocity of flow is much greater in the arterioles than it is in the capillaries normally, and the size of the lumen is determined, within limits, by the tone of the vessel. The tone of the arterioles constantly is under the control of the vasomotor center. This center is in the floor of the fourth ventricle, at the level of the apex of the calamus scriptorius. The thoracic and the upper two lumbar segments of the spinal cord are supplied by fibers which pass down the cord from this center. These fibers end in the gray matter of the lateral horn in connector cells of the sympathetic system.

Vasoconstrictor fibers of the sympathetic nerves arise from these connector cells. Some vasodilator fibers are found in these sympathetic nerves, as well as in the posterior nerve roots.

50 Mylius, K. Funktionelle Veränderungen am Gefässsystem der Netzhaut, Berlin, S. Karger, 1929.

51 Koyanagi, Y. Veränderungen auf der Netzhaut bei Hochdruck. Pathologische Anatomie, Tr. Internat. Cong. Ophth. (1937) 1:145-283, 1938.

52 Fritz, M. Rapport des pressions sanguines humérales et rétiniennes, Bull. Soc. belge d'opht. 67:67-75, 1934.

53 Pal, J. Ueber die kinetische und die tonische Gefässverengung, Med. Klin. 25:702 (May 3) 1929.

Sympathetic vasomotor nerves have been demonstrated in nearly all organs and tissues, including, more recently, the pia mater and the substance of the cortex of the brain (Cobb and Talbott,<sup>54</sup> Forbes<sup>55</sup> and Forbes and Wolff<sup>56</sup>). Vasoconstrictor nerves are supplied to the eye through the cervical sympathetic nerves, however, no vasodilator fibers have been demonstrated anatomically in the eye, although the sympathetic fibers can be followed, through the nerve of Tiedemann, to the retinal vessels and to the uveal vessels (Duke-Elder<sup>26</sup>). Langley and Anderson<sup>57</sup> and Henderson and Starling<sup>58</sup> have proved the constricting effect of these nerves on the uveal vessels. The choroidal vasculature comprises approximately 80 per cent of the intraocular circulation (Duke-Elder<sup>26</sup>). Duke-Elder<sup>29</sup> suggested that the capillary bed of the choroid constricts to lower that intraocular tension when increased systemic arterial pressure has been effected by large doses of solution of epinephrine hydrochloride (1:1,000).

Vasoconstricting and vasodilating activities of the retinal vessels usually have been investigated together. It is not definitely established whether there is increased peripheral resistance in diffuse arteriolar disease with hypertension. The plethysmographic investigations of Prinzmetal and Wilson<sup>60</sup> and Pickering<sup>61</sup> indicate that, while constriction of the peripheral arterioles does occur, the constricting mechanism is independent of the vasomotor nervous system, since anesthetization of the nerves of the latter does not result in

54 Cobb, S., and Talbott, J. H. Studies in Cerebral Circulation. II. Quantitative Study of Cerebral Capillaries, Tr. A. Am. Physicians 42:255-262, 1927.

55 Forbes, H. S. The Cerebral Circulation. I. Observation and Measurement of Pial Vessels, Arch. Neurol. & Psychiat. 19:751-761 (May) 1928.

56 Forbes, H. S., and Wolff, H. G. The Cerebral Circulation. III. The Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. 19:1057-1086 (June) 1928.

57 Langley, J. N., and Anderson, H. K. On the Mechanism of the Movements of the Iris, J. Physiol. 13:554-597, 1892.

58 Henderson, E. E., and Starling, E. H. The Influence of Changes in the Intra-Ocular Circulation on the Intra-Ocular Pressure, J. Physiol. 31:305-319 (Aug. 22) 1904.

59 Duke-Elder, W. S. Recent Advances in Ophthalmology, Philadelphia, P. Blakiston's Son & Co., 1934, p. 115.

60 Prinzmetal, M., and Wilson, C. The Nature of the Peripheral Resistance in Arterial Hypertension with Special Reference to the Vasomotor System, J. Clin. Investigation 15:63-83 (Jan.) 1936.

61 Pickering, G. W. The Problem of High Blood Pressure in Man, Proc. Staff Meet., Mayo Clin. 14:310-320 (May 17) 1939.

vasodilatation Cusick,<sup>62</sup> in 1939, reviewed this field of investigation in his study of the changes in the caliber of the retinal arterioles of patients during an induced vasospastic reaction. He concluded with Herrel<sup>13</sup> that transitory reductions in caliber of the retinal arterioles occur with general vasopressor reactions to cold and tobacco in certain subjects. Contradictory observations have been reported, but, in the main, experimental evidence and clinical experience appear to be in agreement that there exist vasoconstrictor fibers to the retinal vessels and that vasodilator fibers probably also are present. The recent observations of Cusick, Benson and Boothby,<sup>25b</sup> however, suggest that the retina also possesses an autoregulatory mechanism for the control of its circulation.

Wagener,<sup>12</sup> in 1931, was able to demonstrate a measurable dilatation of the retinal arterioles on postoperative examination in 75 per cent of the eyes of 37 patients in whom the inferior cervical and the first and second thoracic sympathetic ganglions and their intervening trunks had been removed. The veins in 52 per cent of the eyes were found to be dilated, but it was noted that the retinal vessels tended to regain their tone within one year after the operation. It is of significance in this connection that notably better results were reported by Wagener, Cusick and Craig<sup>63</sup> in the surgical treatment of hypertensive disease in the patients whose retinal arterioles lacked structural change than in patients with advanced retinal arteriosclerosis. Lobeck,<sup>20</sup> in 1937, was able to demonstrate measurable dilatation of retinal arterioles immediately subsequent to the subcutaneous injection of acetylcholine, choline and theophylline ethylenediamine in human subjects. Recently, I have observed appreciable (measurable) dilatation of the retinal arterioles in man subsequent to administration of theophylline ethylenediamine following coronary anginal pain induced by breathing a mixture of low oxygen concentration. The vessels were observed prior to inhalation of the gas, and narrowing was seen. The administration of the drug immediately was followed by smooth, generalized dilation to a diameter slightly greater than that observed before the gas was inhaled. This change was transient.

Contraction of the ocular arterioles usually accompanies rises in systemic blood pressure,

causing a decrease in the total flow of blood through the eye and a fall in capillary pressure. Thus, there occurs no increase in the intraocular tension. Duke-Elder<sup>20</sup> stated that there is less pronounced vasoconstriction of the arterioles of the eye than of those elsewhere in the body when elevation of the blood pressure is brought about by posterior pituitary injection U S P and that the increase in blood pressure, therefore, is transmitted to the capillary bed, with a resultant passive following of the blood pressure by the intraocular tension.

In general, the normal systemic blood pressure is maintained by the adjustment of the capacity of the peripheral vascular bed to the volume of the circulating blood. The latter is a constant, and the former is a variable. The vasomotor center, by controlling the activity of the arterioles in the unaffected parts, compensates for the local variations in vascular capacity.

Wagener and Keith,<sup>32</sup> in discussing the mechanism involved in the production of pathologic elevation of blood pressure, stated

In any discussion of the abnormal physiologic processes which may give rise to hypertension, four obvious factors must be considered, namely, (1) increased cardiac output, (2) increased viscosity, (3) increased total blood volume and (4) increased resistance in the peripheral circulation.

The increase of resistance to the flow of blood in the peripheral circulation in cases of systemic arterial hypertension, according to Pal,<sup>53</sup> is the result of widespread, continuous hypertonus. Prinzmetal and Wilson,<sup>60</sup> among others, supported the conception of a generalized vasoconstriction of the small arteries and arterioles associated with essential hypertension and with chronic nephritis. Wagener<sup>49a</sup> stated the opinion that this is a functional narrowing of the lumen of the arterioles, at least in the earlier phases of the development of the pathologically elevated blood pressure, and that structural changes in the walls of these small arterial vessels are not demonstrable during this period. The reduction in caliber of the retinal arterioles in this condition of continuous hypertonus may be observed with the ophthalmoscope as essentially a smooth, generalized narrowing, which may differ in degree in the several vessels under observation but which will be uniform throughout the course of a particular arteriole.

The observations of Cusick and Herrel<sup>13</sup> suggest that this smooth narrowing may be considered to be due to an increase in vasomotor tone, probably brought about by excessive sympathetic vasoconstrictor stimulation. That the arteriolar contraction, on the other hand, may

62 Cusick, P. L. *Changes in the Retinal Arterioles of Patients During an Induced Vasospastic Reaction*, Thesis, University of Minnesota Graduate School, 1939.

63 Wagener, H. P., Cusick, P. L., and Craig, W. M. *The Retina in Surgical Cases of Primary Hypertension*, *Tr. Am. Ophth. Soc.* **37**: 379-394, 1939.

be the result of a direct action of a vasopressor substance on the walls of these vessels is the view expressed by Volhard,<sup>64</sup> by Goldblatt and his followers<sup>48</sup> and by Pickering.<sup>61</sup> It has been demonstrated ophthalmoscopically by Lobeck,<sup>20</sup> Neame,<sup>14</sup> Badtke<sup>22</sup> and others that, however the constriction is produced, the retinal arterioles become generally narrowed fairly proportionally to the severity of the hypertensive disease and, presumably, to the increased elevation of the systemic blood pressure.

The persistence of elevation of blood pressure in persons with diffuse vascular disease results in the production of ophthalmoscopic signs which probably are indicative of the development of hypertrophy of the media of the arterioles. This is the most common histologically observed structural change in the arteriolar walls of persons with chronic hypertensive disease. Sclerosis of these walls of the medial or of the intimal type ultimately will ensue, and that its development probably does have some effect in narrowing the lumen of the arterioles in hypertensive persons is suggested by certain observations in my study of the retina in cases of hypertension, in 1941.<sup>11</sup>

The end stages of hypertensive disease and of nephritis are essentially similar, although they may be reached through various primary modes of development, as Wagener and Keith<sup>32</sup> have stated. The same basic processes logically may be assumed to be concerned in the production of the retinal and of the renal complications. The ophthalmoscopic differentiation of the retinal changes of hypertension from those of nephritis probably lies in the sequential development of the various factors comprising the terminal picture rather than in the final histologic picture. Efforts to differentiate clinically these various systemic vascular diseases have stimulated ophthalmoscopic study of the retina and of the retinal vascular lesions as an aid to diagnosis, and the presence of such signs may also be of prognostic and therapeutic value.

Gowers,<sup>65</sup> in 1876, in studying the retinal vessels ophthalmoscopically in the absence of retinitis, appears to have been the first to employ the ophthalmoscope as an aid in diagnosis of systemic vascular disease. He wrote:

When in chronic Bright's disease, the pulse is incompressible, there may as a rule be seen reduction in size of the retinal arteries independently of any retinal disease, and this reduction in size is fairly proportionate to the increased arterial tension.

Gowers apparently was the first to express the opinion that the reduced caliber of the retinal arteries was due to constriction of the vessels, when he stated:

When the retina is free from local disease, there is no reason to believe that the retinal artery and vein differ in their condition from other arteries and veins of the same size, and, therefore, any marked change in their state apart from cerebral or ocular disease may be taken as evidence of a similar change throughout the vascular system.

There is, of course, nothing in the fact that the retinal arteries are small in Bright's disease, it has long been remarked as a common feature in albuminuric retinitis, but it is usually regarded as a consequence of the retinal change, and the points on which I would insist are that it occurs also quite independently of the retinal change and stands commonly in direct relation to another condition, the blood tension.

Wagener and Keith<sup>32</sup> stated "In essence, these statements cover the recognized significance of retinal vascular lesions in systemic disease today." The relation of the retinal lesions to general vascular disease and the significance of the ophthalmoscopic signs of arteriosclerosis were studied and interpreted by Raehlmann,<sup>66</sup> Gunn<sup>67</sup> and Rohmer<sup>68</sup> in 1889, 1892 and 1906, respectively, and have been investigated by others since then. The concept of retinal arteriosclerosis as a part of general and cerebral arteriosclerosis grew in concept, and it has become increasingly accepted in recent years "that the lesions observed ophthalmoscopically in the retinal arterial branches are really arteriosclerotic in their characteristics and systemic significations."<sup>32</sup> O'Hare and Walker,<sup>69</sup> in 1924, pointed out that, almost without exception, so-called retinal arteriosclerosis is a part of hypertensive disease and diffuse arteriosclerosis and not of atherosclerosis. Parenthetically, it was O'Hare,<sup>70</sup> in 1920, who pointed out the marked lability of the systemic blood pressures in moderately advanced hypertensive disease.

66 Raehlmann, E. Ueber ophthalmoskopisch sichtbare Erkrankung der Netzhautgefasse bei allgemeiner Arteriosklerose, mit besonderer Berucksichtigung der Sklerose der Hirngefasse, *Ztschr f klin Med* **16** 606-654, 1889.

67 Gunn, R. M. Ophthalmoscopic Evidence of (1) Arterial Changes Associated with Chronic and Renal Disease, and (2) of Increased Arterial Tension, *Tr Ophth Soc U Kingdom* **12** 124-125, 1892, On Ophthalmoscopic Evidence of General Arterial Disease, *ibid* **18** 356-381, 1898.

68 Rohmer, J. Rapport sur l'artério-sclerose oculaire, Paris, G. Steinheil, 1906.

69 O'Hare, J. P., and Walker, W. G. Arteriosclerosis and Hypertension, *Arch Int Med* **33**:343-349 (March) 1924.

70 O'Hare, J. P. Vascular Reactions in Vascular Hypertension, *Am J M Sc* **159** 369-380 (March) 1920.

64 Volhard (footnotes 45 and 46)

65 Gowers, W. R. The State of the Arteries in Bright's Disease, *Brit M J* **2**:743-745 (Dec 9) 1876.

Wagener and Keith, together with their co-workers and followers, in the past two decades have evolved a logical and useful clinical classification of hypertensive disease in the absence of an established etiology. These workers began their joint studies in 1920 with the clinical recognition of a case of so-called malignant hypertension. The patient had been admitted to the hospital with a diagnosis of chronic glomerulonephritis. Typical "albuminuric retinitis" was present, but renal function was far too good for a patient with terminal chronic diffuse nephritis. These workers, by further clinical, ophthalmologic and pathologic studies, identified a syndrome characterized by hypertension and diffuse arteriolar changes throughout the body. A small series of cases of this syndrome was presented in 1924,<sup>71</sup> and Keith, Wagener and Kernohan,<sup>72</sup> in 1928, reported a series of 81 cases in greater detail. In many of these cases the diagnosis frequently had been made prior to the development of serious impairment of the cardiac, renal, cerebral and retinal functions, and it was in this respect that the condition differed from the *bosartig* hypertension of Volhard<sup>46</sup> and the malignant nephrosclerosis of Fahr.<sup>73</sup> The retinal changes in the cases reported by Keith and by Wagener, individually or as co-authors, differed in degree from one patient to another, but certain distinctive changes always were present. The disease rapidly progressed, and, in their 1928 series, 78 per cent of the patients had died within a period of one year.

Another group of cases of hypertensive disease gradually came to be recognized in which the course was less rapid, remissions sometimes occurred and there existed mild vasospastic retinitis. The retinitis always was an important diagnostic feature. There came to be recognized also, a group in which marked hypertension existed without a demonstrable break in the functions mentioned but in which there was present more advanced narrowing and sclerosis of the retinal arterioles than in the cases of truly "benign," "simple" hyperpiesia. The authors preferred to designate these four groups by numbers rather than apply to them confusing descriptive terms. Thus, they termed as group 1 the cases of the usual, benign form, as group 2, cases

in which there was more marked hypertension but few untoward symptoms and no retinitis, as group 3, the cases in which mild vasospastic retinitis existed and as group 4, the cases in which the syndrome of so-called malignant hypertension was present.<sup>74</sup> It is of interest to mention here that cases of chronic glomerulonephritis originally were designated as group 1 by Keith, Barker and Kernohan,<sup>75</sup> in 1931, and that the present group 4 was called group 5. The present classification of primary, or essential, hypertension into four groups was first used by Keith, in 1932.<sup>76</sup> Cases of acute vasospastic hypertension was added to this group of hypertension in the exhibit offered by Keith and Wagener in 1934 (personal communication).

Keith<sup>76</sup> applied the prefixing phrase of diffuse arteriolar disease with hypertension to the numerical groupings in 1932, and these authors and their co-workers and followers have continued to employ this clinical terminology and classification in the diagnosis of hypertensive disease. The degree of narrowing and sclerosis of the retinal arterioles, as observed with the ophthalmoscope by these workers, also is graded from 1 to 4, depending on the intensity of the changes seen.

Wagener and Keith<sup>32</sup> stated

Clinical differentiation of the four groups is usually not difficult. Patients of groups 1 and 2 necessarily must have good retinal, cerebral, cardiac and renal function, whether the hypertension be labile, or high, with a tendency to fixation. In cases of group 3 there is evidence of dysfunction of one or of several of the organs belonging to the arterial system, while in group 4 these functional disturbances become more definite and final failure may occur because of a simultaneous serious interference in the blood supply to the retina, brain, heart and kidneys. A given case may be markedly progressive and pass from group 1 to group 4 in a short period. On the other hand, there are cases in which there is little progression over a period of many years, the majority of these belong to group 1 but a moderate number to group 2 and a few to group 3. Because the arterioles throughout the organs of the body seem to be the chief point of attack and can be readily visualized only in the retina, the findings obtained by the ophthalmoscope are very important.

A further report on an increased number of cases of essential hypertension recently has been

71 Wagener, H. P., and Keith, N. M. Cases of Marked Hypertension, Adequate Renal Function and Neuroretinitis, *Arch Int Med* **34** 374-387 (Sept.) 1924.

72 Keith, N. M., Wagener, H. P., and Kernohan, J. W. The Syndrome of Malignant Hypertension, *Arch Int Med* **41** 141-188 (Feb.) 1928.

73 Fahr, T. Ueber Nephrosklerose, *Virchows Arch f. path. Anat.* **226** 119-178 (June) 1919.

74 Wagener, H. P. The Clinical Interpretation of Retinal Vascular Lesions in Hypertension and Nephritis, *Pennsylvania M. J.* **40** 705-711 (June) 1937.

75 Keith, N. M., Barker, N. W., and Kernohan, J. W. Histologic Studies of the Arterioles in Various Types of Hypertension, *Tr. A. Am. Physicians* **46** 66-68, 1931.

76 Keith, N. M. II Cardiovascular Diseases in Relation to the Retina, *Tr. Am. Acad. Ophth.* **37** 37-49, 1932.



published by Keith, Wagener and Barker.<sup>77</sup> The classification just mentioned was employed and conclusions were drawn with regard to the prognosis in 219 cases, representing all four groups. An actuarial survival curve reveals that there is a death rate of 10 to 12 per cent within a period of one year following the time of the first examination in groups 1 and 2. This is in contrast to the 35 per cent mortality in group 3 and the 79 per cent in group 4 in the same length of time.

## COMMENT

"Normal blood pressure" in the human being is somewhat difficult of accurate definition in terms of millimeters of mercury. From his sta-

of the age of the patient. These figures for the upper limits of normal clinical blood pressures in the human being are those accepted by most workers in this field.

Blood pressure, as Mountain and Allen<sup>79</sup> recently have reemphasized, is not a static, but a labile, manifestation of physiologic activity of the human body. These authors concluded, in their studies on the fluctuation of blood pressure in patients with essential hypertension, that the pressure varies widely in the individual cases and that the greatest fluctuation occurs in groups 2 and 3 because of the pronounced elevation of the blood pressure with relatively little fixation of it in these groups. Since, as is known, normal blood pressure fluctuates only within rather nar-

TABLE 4—Mean Caliber of Retinal Arterioles in Microns as Measured by Various Authors

Keith Wagener <sup>22</sup> Classification	Volhard <sup>17</sup> Classification	Lo Cascio <sup>18</sup>	Wagener <sup>12</sup>	Neume <sup>14</sup>	Lobbeck <sup>20</sup>	Kuhn <sup>21</sup>	Badtke <sup>22</sup>		Koch <sup>11</sup>	
							Range	Mean	Range	Mean
Normal blood pressure	Normal blood pressure	110 to 120	50 to 120	86 to 94	88 to 150	86 to 138	90 to 112	105	47 to 140	91
Group 1	"Red" hypertension				74 to 127		100 to 145	117	46 to 124	77
Group 2	Transition forms						60 to 85	70	31 to 111	67
Group 3	"Pale" hypertension				27 to 58				31 to 111	60
	Genuine nephrosclerosis									
Group 4	Primarily contracted kidney						60 to 91	70	31 to 94	41
	Genuine nephrosclerosis with albuminuric retinitis				26 to 33					
	Malignant hypertension				53 to 81					
Chronic glomerulonephritis with normal brachial diastolic blood pressure							96 to 125	109	47 to 124	84
Chronic glomerulonephritis with elevated brachial diastolic blood pressure					38 to 73		60 to 78	70	37 to 93	60

tistical study of human blood pressures in 2,282 men and 3,258 women, Wetherby<sup>78</sup> reached the conclusion that it was impossible to draw a definite line between normal and elevated or depressed pressures on the basis of single readings. Variations in pressures in states of health occur within narrow limits under conditions of exercise, emotion and similar stresses. Blood pressures which consistently are higher than 150 mm of mercury systolic and 90 mm of mercury diastolic usually are interpreted as indicating the existence of pathologic hypertension regardless

of the limits in most cases, these authors found comparatively slight variations in group 1 because the elevation of the systemic pressure was not great. Similarly, in cases of hypertension, group 4, the fluctuation also was slight, but only because the systemic pressure was relatively fixed. They stated the opinion that the soundness of grouping cases of hypertension on the basis of retinal changes is confirmed by the existence of progressive elevation of both the maximal and the minimal brachial systolic and diastolic blood pressures in each of the four successive groups of hypertension classified according to the criteria of Keith and Wagener.

Values for similar fluctuations of the brachial and of the retinal diastolic blood pressures were

<sup>77</sup> Keith, N. M., Wagener, H. P., and Barker, N. W. Some Different Types of Essential Hypertension. Their Course and Prognosis, *Am J M Sc* **197** 332-343 (March) 1939.

<sup>78</sup> Wetherby, M. A Comparison of Blood Pressure in Men and Women. A Statistical Study of 5,540 Individuals, in Berglund, H., and Wedes, G. *The Kidney in Health and Disease*, Philadelphia, Lea & Febiger, 1935, pp. 370-386.

<sup>79</sup> Mountain, G. E., and Allen, E. V. Vascular Clinics. XV. Fluctuation of Blood Pressure in Essential Hypertension, *Proc Staff Meet, Mayo Clin* **16**: 260-263 (April 23) 1941.



not sought in the individual cases in my study<sup>11</sup>, however, the fact that variations probably occur is indicated by the range of values obtained with reference to the caliber of the arterioles and the systemic and local blood pressures recorded. Rather wide variations in arteriolar caliber have been reported by others (tables 2 and 4). No previous studies have been made, however, in an attempt to correlate the diameters of the retinal vessels with both the systemic and the local ocular blood pressure, nor, apparently, have the previous investigations been carried out on large numbers of arterioles in sufficiently representative groups of patients. That this may not always be necessary, however, is indicated in these tables with regard to the values reported by other investigators for normal retinal arterioles and without reference to the particular device employed in obtaining these measurements. The mean value has not always been given by each author, however, it will be observed that not only the range but the mean, when given, are in rather general agreement.

There exists only two reports (Lobeck,<sup>20a</sup> Badtke<sup>22</sup>) concerning retinal vascular diameters in cases of hypertensive disease, and these are somewhat difficult to evaluate with reference to my study<sup>11</sup> because the authors employed the classification of Volhard.<sup>45</sup> In the main, however, as will be observed in table 4, the values given by Lobeck<sup>20</sup> and by Badtke<sup>22</sup> correspond to those I obtained, although these values do not approximate each other quite as well as do the figures given by the various workers for normal values.

The mean caliber of the retinal arterioles, as well as the range of calibers, in my study generally is more in accord with the values given by Lobeck than with those obtained by Badtke, although both these workers used the heliometer apparatus devised by the former. No effort was made in my study to differentiate "red" and "pale" hypertension as such or to distinguish specifically the "transition forms." Since it is believed, with Wagener and Keith, that an angiospastic tendency is present in practically all cases of hypertension, it is difficult, on the basis of vascular physiology, to correlate dilatation of the arterioles with a moderate increase in brachial systolic blood pressure even in the

presence of a normal systemic diastolic blood pressure.

Badtke obtained a mean retinal arteriolar caliber of 117 microns for 56 patients with "red" hypertension. This figure represented a range of 100 to 145 microns, and, for the most part, he measured only the superior temporal arterial vessels at the margin of the disk. His figures for "red" hypertension, as will be seen in table 4, are greater than those obtained in his series of 25 normal patients, otherwise the values obtained by Lobeck and by Badtke in cases of the various forms of hypertensive and nephritic disease appear to be in general agreement with mine.<sup>11</sup>

It is possible that Badtke, with reference to "red" hypertension, encountered a group of patients who might better have been classified as having diffuse arterial disease with atherosclerosis, but he did not give the actual figures for the systemic blood pressures in this group, of 56 patients. It might be reasonable to suppose that relative retinal vascular widening in relatively elderly patients may accompany increases in brachial systolic blood pressures, particularly if the elasticity of the larger arteries had been diminished. It is possible, also, that Fritz<sup>52</sup> encountered a similar group of patients, after the study of which he advanced, among others, the theory that certain vascular regions exist in which the arterioles fail to contract to a sufficient degree. He expressed the opinion that the blood thus will enter the capillaries under too great a pressure and that this would permit hemorrhagic and serous transudation through the capillary walls. He also assumed that there might be a more or less uniform degree of arteriolar attenuation in some stages of hypertensive disease and that this would permit uniform optimal perfusion of the retinal capillaries without the development of retinitis. The arterioles are constricted unequally in other stages, he thought, so that the blood in the capillaries would enter under too low a pressure and result in infarction. Fritz supported this hemodynamic or mechanical theory by numerous observations on the retinal pulse and the intraocular blood pressure reactions. His hypotheses have not yet been proved.

60 East Seventy-Fifth Street

## News and Notes

EDITED BY DR W L BENEDICT

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### GENERAL NEWS

**Research Study Club of Los Angeles**—The Research Study Club of Los Angeles announces its fifteenth annual mid-winter postgraduate clinical assembly in ophthalmology and otolaryngology, Jan 21 to Feb 1, 1946, and special courses in applied anatomy and cadaver surgery of the head and neck, February 1 to 5. Guest speakers for ophthalmology and their subjects are Dr Alan C Woods, immunology in ocular disease, Dr Jack S Guyton, newer methods of surgical approach in ophthalmic surgery, Dr Meyer Wiener, demonstrations in surgery of the eye, Dr Frederick C Cordes, recent advances in ophthalmology, and Mr Irving B Lueck, analysis of various optical problems, with special reference to lenses. Dr Herbert M Evans, professor of biology at the University of California, at Berkeley, Calif, will discuss recent advances in nutrition in relation to problems of the eye, ear, nose and throat, with particular reference to nicotinic acid and riboflavin deficiencies in man.

Applications should be made to Pierre Viole, M D, 1930 Wilshire Boulevard, Los Angeles 5.

**Research Project in Cause of Blindness Due to Onchocerciasis in Guatemala**—Dr William B Clark, professor of ophthalmology, Tulane University of Louisiana School of Medicine, has just returned from Yepocapa, Guatemala, where he spent six weeks instituting a research project in the cause of blindness in patients with onchocerciasis in Guatemala. This project is spon-

sored jointly by the Caribbean Sector of the Pan American Sanitary Bureau and the Department of Health of Guatemala. The project is being continued in Dr Clark's absence by Dr. Bertha Riveroll Noble, of México, D F, who was a former Pan American Kellogg Foundation Fellow in Ophthalmology at Tulane University from 1943 to 1945. Dr Clark will return to Guatemala in January 1946, to close out or continue the project, as the results of the investigation justify.

**Pan-American Congress of Ophthalmology.**—The Pan American Airways, Inc, is offering a 15 per cent reduction on fares to delegates attending the Pan-American Congress of Ophthalmology at Montevideo, Uruguay.

The fare from Miami to Montevideo is \$486 one way or \$874.80 round trip, if traveling via the east coast, and \$504 one way or \$907.20 round trip, if traveling via the west coast.

For any delegates who may be interested in making a circle trip around South America the fare will be \$891.

All these fares are subject to 15 per cent United States transportation tax. However, as already mentioned, these fares are also subject to 15 per cent discount.

**"Lectures on Motor Anomalies"**—A third printing of Alfred Bielschowsky's "Lectures on Motor Anomalies" is now on sale at Dartmouth College Publications, Hanover, N H, at \$1.50 per copy, postpaid.

## Obituaries

N BISHOP HARMAN, M B

1869 — 1945

Bishop Harman was born in London and received his education at Cambridge and at Middlesex Hospital, where he qualified in medicine and became a Fellow of the Royal College of Surgeons in 1898. He was one of the first to become interested in the prevention of blindness and in the education of children with defective eyesight after the unrelieved defects of vision were noted in school children. He was instrumental in instituting compulsory notification of cases of ophthalmia neonatorum. Harman was one of the oculists appointed to superintend the regular testing of children's eyesight, and he instituted a number of reforms, such as cessation of sewing by artificial light and the use of slates and pencils. As ophthalmic consultant to the London County Council, he recognized the need for separate classes for children with high myopia. These sight-saving schools were established in London in 1908 and were fitted out with special desks and apparatus. These methods

were adopted in the English provincial centers and were followed in the United States. Improved standards of lighting and of school books were devised through Harman's endeavors, and he was one of the main contributors in the diminution of visual defects from preventable causes in childhood.

Harman was president of the section of ophthalmology of the *British Medical Journal* meeting at Winnipeg, in 1930. In addition to writing his excellent "Aid to Ophthalmology," he devised a number of new and ingenious instruments for ophthalmologists. His last interest was in testing night vision, which in the recent war was of such importance. He constructed a simple but practical apparatus for this examination. In his long connection with the *British Medical Journal* he was one of its most active members and served as treasurer for fifteen years.

ARNOLD KNAPP

## Correspondence

### MARFAN'S SYNDROME

*To the Editor* —The August 1945 issue of the ARCHIVES, page 112, carries a paper entitled "Marfan's Syndrome with Unusual Complications," by Dr. James L. McGraw.

One feels that the title does not harmonize with the contents of the paper, the unusual complications do not have a casual connection with the anomaly but are only postoperative complications of extraction of the lens in a given case of Marfan's syndrome. In the opening paragraph it is stated that Marfan described, in 1896, the case of a young girl with the symptom complex of arachnodactyly and ectopia lentis. The statement is erroneous. In my paper on Marfan's syndrome (ARCH OPHTH 27:477 [March] 1942), I pointed out that the knowledge of congenital dislocation of the lens and arachnodactyly began with the observation of Marfan, who noted a peculiar and until then undescribed symmetric malformation of the four extremities in a 5½ year old girl. The malformation was characterized by elongation of the bones and a certain degree of attenuation, more pronounced in the distal parts. There were contractures of the fingers, poor musculature, pronounced deficiency of subcutaneous fat and, fur-

thermore, a considerable spur of the os calcis. Marfan described the fingers and toes as "spider-like" and called the syndrome *dolichosténomelie*. In Marfan's case and, similarly, in the other cases of the early literature there is no mention of ocular symptoms. Boerger's report (1914) was the first in the literature to call attention to the presence of the characteristic symptoms of congenital luxation of the lens and iridodonesis with enlarged cornea and hydrophthalmos. Poynton and Maurice demonstrated a case before the Medical Society of London in 1923, and in the discussion following the report "a member of the medical society" spoke of a patient under his care who had the identical syndrome, but with congenital dislocation of the lenses also. The first paper to emphasize the importance of ocular symptoms is that of Ormond and Williams (1924).

Marfan, in 1896, described only the typical habitus of the body, that the congenital dislocation of the lens is part of the syndrome became known only much later and through the observation of other authors.

ANDREW RADOS, M D, NEWARK, N J

31 Lincoln Park (2)

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

## Congenital Anomalies

A CONTRIBUTION TO THE STUDY OF ANOPHTHALMIA WITH DESCRIPTION OF A CASE T ROGALSKI, Brit J Ophth 28:429 (Sept) 1944

The anomaly was seen in a full term male child who died of military tuberculosis of "nearly all the organs" at the age of about 10 weeks. The left side of the mouth was enlarged, and there was a V-shaped cleft pointing to the left orbit and connected with it by a slight groove in the skin. Another groove extended from the right angle of the mouth to the right ear, the right two thirds of the upper jaw, i. e., the part to the right of the harelip, projected beyond the mandible, and the nose slanted downward to the right. The right orbit and eyeball appeared normal, but there was no sign of the left eyeball. No malformations were noted in any other region of the body.

Rogalski suggests that in all cases in which the essential parts of the eye, i. e., the retina proper and the lens, are lacking, whether the mesodermal constituents and the pigment epithelium are present or not, the term anophthalmia should be employed. The term microphthalmia should be reserved for cases in which all the ocular constituents, including the retina proper (or the optic nerve) and the lens, are present either underdeveloped or malformed or only vestigial.

Anophthalmia thus defined, may be classified into two types. 1 Complete anophthalmia, in which no vestiges of the optic outgrowth can be found. In cases of this type it cannot be determined whether the optic vesicle has been formed and suffered complete atrophy or has never been formed at all. 2 Consecutive anophthalmia in which an optic vesicle or cup has certainly been formed but has atrophied in the very early stages, leaving, as its vestige, more or less malformed pigment epithelium. Each type may be bilateral or unilateral, and both are almost certainly of genetic origin, the fault being in the neuroblast itself or in other tissues, e. g., in the hematogenic mesoderm, with disturbance of the blood supply.

The author's case belongs to the second type of anophthalmia so defined, and not to the third type described by Ida Mann, as according to her definition it would

The article is illustrated

W ZENTMAYER

CASUISTIC CONTRIBUTION TO THE MARCUS GUNN SYNDROME M ARTIGAS and V A VICTORIA, Arch de oftal de Buenos Aires 19: 101 (Feb) 1944

Two atypical cases of this syndrome are reported. One patient, a girl 17 years of age, had no ptosis of the superior lid, but when the mandible was lowered the left upper lid would rise. The other patient, a boy 10 years of age, with congenital ptosis of the left upper lid, showed elevation of the ptosed lid on swallowing. In his case the synergism was between the third and the ninth nerve. The article is illustrated.

H F CARRASQUILLO

## General Diseases

RUBEOSIS IRIDIS DIABETICA F B FRALICK, Am J Ophth 28:123 (Feb) 1945

Fralick refers to the work of Salus and Kurz, and notes the interesting features of rubeosis iridis diabetica. He reports 5 cases. One patient, a young person, had severe diabetes with hypertension and extensive damage to the kidneys, 2 patients, elderly, were diabetic and hypertensive, 2 were nondiabetic, both having hypertension and an intraocular melanoma, and 1 had a condition which was diagnosed clinically as an old occlusion of the central retinal vein. The only feature presented by all the patients was the obvious circulatory disturbance, of such a degree that rubeosis iridis and hemorrhagic glaucoma developed. Rubeosis iridis has thus been observed in patients showing rather varied pathologic conditions.

The author cannot support the contention that rubeosis iridis is a manifestation of an ocular syndrome seen in its true form only in diabetic persons. He believes that, given the right pathologic changes in the vascular supply to the eyeball, metabolic abnormalities become established which promote a low grade iritis, with formation of new vessels and secondary peripheral root synechias, resulting eventually in hemorrhagic glaucoma.

W ZENTMAYER

OPHTHALMOSCOPY AND THE DIAGNOSIS OF HUMAN ILLNESS A J BEDELL, Am J Ophth 28:139 (Feb) 1945

In this Jackson Memorial Lecture, before the Colorado Ophthalmological Society, Bedell speaks of Edward Jackson's useful life and enumerates a number of ocular conditions and their importance in relation to general health.

W S REESE

## Glaucoma

DEEP-CHAMBER GLAUCOMA DUE TO THE FORMATION OF A CUTICULAR PRODUCT IN THE FILTRATION ANGLE A B REESE, *Am J Ophth* 27:1193 (Nov) 1944

Reese gives the following summary

"The endothelium of the anterior chamber may form a cuticular product at any site where it is normally found. It may also grow and produce this product over sites where it is not normally found, such as, over the trabeculae, across the pupillary area, or along the posterior surface of the iris. When this cuticular product is formed over the inner surface of the trabeculae or in the interstices of the trabeculae, glaucoma may ensue. This may occur as a primary disease with no apparent provocation. It also may occur as a result of inflammation in the anterior chamber, or as the result of trauma to the eye. The endothelial changes occur on the posterior surface of the cornea and permit aqueous to enter the corneal stroma. This gives rise to edema and its sequelae, such as vesicles, bullae, pannus, keratitis, and ulcer. The increased intraocular pressure intensifies these corneal changes. The underlying pathologic change and clinical picture are similar to dystrophia epithelialis corneae on the one hand, and the corneal changes consequent to glaucoma on the other hand, except that in this condition both factors are present and therefore the cornea may dominate the clinical picture."

W S REESE

ROENTGEN IRRADIATION OF CERVICAL SYMPATHETIC TRUNK IN TREATMENT OF GLAUCOMA J CASANOVAS, *Arch Soc oftal hispano-am* 4:594 (July-Aug) 1944

After discussing fully this method of treatment, the author concludes that roentgen irradiation of the cervical portion of the sympathetic trunk is useful only as a preliminary measure to prepare for an operation in cases in which the visual field is greatly contracted and the fixation point is menaced. In these cases the field may be improved so as to make the operation possible without endangering the visual acuity. The author further states that the method is useful also as a palliative measure in cases in which there is very high tension and as a preliminary to operative procedures in these cases.

H F CARRASQUILLO

## Injuries

TREATMENT OF PERFORATING OCULAR INJURY L H SAVIN, *M Press & Circ* 209:134 (March 3) 1943.

After comments on sympathetic ophthalmia and its prevention, indications for early enucleation are given. The composition of an intra-

ocular foreign body is important. The patient may know what metal he was working with, and a sample is often available. Of importance is whether the foreign body is magnetizable or not. Foreign bodies can be accurately localized by localizing roentgenograms, and the author especially mentions the Spaeth ring method. The chemical action of a foreign body is also important. Gold and quartz are inert. Iron and steel cause siderosis. Copper has a chemical action, with early cataractous changes, of which a posterior cortical cataract is significant. Most of the other foreign bodies have slow chemical action. Glass may remain quiet for ten or fifteen years, though sometimes it causes a violent reaction. The effect of organic foreign bodies is also variable. A particle of coal may remain stationary for ten years. Eyelashes may be quiet for many years, unless they form epithelial cysts or pearl tumors. Aluminum alloys were important in World War II, as they are frequently employed in bombs and projectiles. Their chemical effect is under study. Generally they cause mild chemical irritation (iritis, adhesions and lenticular opacities), but necrotic patches have been observed by the author in the retina of man and rabbits. Nonmagnetized tools, steels and cutting tools of tungsten carbide are the present day hazards to industrial workers.

If the foreign body in the interior of the eye is not magnetizable, the question of leaving it alone comes up, as such a body is frequently tolerated for many years. In the case of copper and brass something must be done. An attempt to remove the particle by scleral incision should be made, using a forceps guided by the electric ophthalmoscope. Injured eyes must be kept under observation, as symptoms of sympathetic ophthalmia may develop, with irritability of the injured eye, corneal deposits and an aqueous flare in the second eye. The blood count is of no diagnostic value, as mononuclear leukocytosis is a fallacious guide and is frequently absent in cases of sympathetic ophthalmia. Injections of neoarsphenamine are useful in treatment of sympathetic ophthalmia and are of value as a prophylactic.

ARNOLD KNAPP

## Lens

THE LENS IN ACCOMMODATION J G SINCLAIR, *Am J Ophth* 28:38 (Jan) 1945

Sinclair states that after birth, as the lens grows and, at the same time, functions increasingly in accommodation, stresses are set up tangential to the surface, and the (lens) rods become aligned in sheets. Between the sheets is albuminous liquid. One zone of stress in particular contains more liquid than the rest and separates the nucleus from the surrounding cortex. Tension at the equator, besides slightly stretching the lens, moves back to the axis on both sides of the nucleus. The nucleus is held

in position by strands that cross the liquid-filled zone, but the whole nucleus is moved forward. The force in this axial expansion is furnished partly through cortical elasticity and partly through hydrostatic pressure, probably based on a small differential in osmotic pressure of lenticular fluid over surrounding fluids. The hydrostatic component operates uniformly in all directions, but its effectiveness on any wall varies directly with the radius of curvature and the thickness of that wall. The curved prismatic cortical rods of the lens tend to become straight in turgor and in doing so supply the necessary elastic component. These forces, together with the fact that the central, or pupillary, zone of the cortex is thin, permit the changes in radius of curvature characteristic of accommodation in this region. This change does not extend to the whole lateral face of the lens.

The lenticular structure here pictured is found in the human eye after birth. In old age the liquid space is reduced or obliterated, and the whole lens becomes like the nucleus, an unyielding and highly refracting mass. The theory of elasticity of the lens presented here does not call for modification of accepted theories of accommodation, but it does make plausible the effectiveness of the force of tension on the ligament of the lens. A diagram shows the mature crystalline lens in tension and in relaxation.

W ZENTMAYER

### Methods of Examination

PHOTOMETER FOR MEASURING THE SCOTOPIC CANDLEPOWERS OF SELF-LUMINOUS OPHTHALMIC TEST OBJECTS. W S STILES, *Brit J Ophth* 28: 629 (Dec) 1944

A photometer is described with which the scotopic candle power of feeble light sources (down to about  $10^{-9}$  candles) can be measured. Small spots of radium paint, 2 or 3 mm in diameter and having candle powers in the range covered, are now used (Livingston) to plot the dark-adapted visual field, and the present photometer was designed primarily for their calibration.

A description of the instrument and the conditions of measurement are given.

It may fairly be concluded that, provided the energy distribution of a given test object is roughly matched by choosing a suitable color filter whose computed scotopic transmission is known, an experimental comparison of the test object with the filtered light will give the scotopic value of the test object with satisfactory accuracy, probably to within 12 per cent, except possibly for red test objects. This is true provided the photometric match is made at a scotopic brightness of about  $5 \text{ by } 10^{-4} \text{ e f c}$  (4 mm diameter pupil) and the result is the mean for at least two "normal" observers.

W ZENTMAYER

### Neurology

VISIBLE RETINAL ARTERIOLAR SPASM ASSOCIATED WITH MULTIPLE SCLEROSIS. R BRICKNER and C FRANKLIN, *Arch Neurol & Psychiat* 51: 573 (June) 1944

Abrupt attacks involving various parts of the central nervous system, including the visual apparatus, and usually lasting more than a few minutes or a few hours, are common in cases of multiple sclerosis. However, sudden attacks of one kind or another of brief duration are not uncommon, and the subject of this report is arteriolar spasm associated with such attacks and relief of symptoms with amyl nitrite.

In 2 cases of multiple sclerosis, spasm of the retinal arterioles was coincident with the presence of scotomas. When the scotomas receded or disappeared, the spasm also disappeared, this change followed immediately the inhalation of amyl nitrite in 1 case and was spontaneous in the other. In a third case attacks of blurred vision were promptly relieved by inhalation of amyl nitrite.

R IRVINE

ENCEPHALITIS DUE TO TOXOPLASMA. G SCHWARZ and J WENDELL, *Arch Neurol & Psychiat* 52: 425 (Nov) 1944

Two clinical cases of toxoplasma encephalitis of the so-called latent infantile type are presented.

Both patients were white girls 5 years of age. The first child had severe pneumonia at the age of 9 weeks after which most of her symptoms were first noted. The other child had an illness at birth involving the respiratory tract and congenital dislocation of the hips. Both patients had had convulsive seizures earlier in childhood. The clinical observations were essentially similar. Both patients showed mental deficiency. Visual acuity was greatly reduced, and there was ocular nystagmus. Ophthalmic examination revealed white nerve heads and chorioretinitis, involving particularly the macular areas. Pneumoencephalograms revealed symmetric dilatation of the ventricular systems. Roentgenograms of the skull in each case showed multiple irregular calcifications distributed throughout both cerebral hemispheres, particularly in the occipitoparietal region. A specimen of the blood of the first patient, examined by Dr Abner Wolf, contained antibodies for Toxoplasma.

R IRVINE

### Parasites

HISTOLOGIC CHANGES IN AN EYEBALL WITH CYSTICERCOSIS. E F PERIS, *Arch Soc oftal hispano-am* 4: 98 (Jan-Feb) 1944

Peris studied an enucleated eye involved in the rare condition of cysticercosis. The eye had been treated with diathermy (electrocoagulation).

Macroscopically, the organ showed beginning phthisis bulbi. Histologically, all the layers and



tissues of the eye except the sclera and the cornea were involved in an intense inflammatory process. Important to note was that the choroid did not show changes similar to those of sympathetic ophthalmia, which other investigators have claimed may arise in the other eye in cases of this disease. The pathologic process in this layer was chiefly that of severe *nidocystitis*.

The cestode had undergone calcareous degeneration, as usually happens after its death in the eye.

H F CARRASQUILLO

### Physiology

EFFECTS OF STIMULATION AND LESION OF THE MEDIAN LONGITUDINAL FASCICULUS IN THE MONKEY M BENDER and E WEINSTEIN, Arch Neurol & Psychiat 52 106 (Aug) 1944

Experimental stimulation of the mesial fibers of the median longitudinal fasciculus in the monkey causes ocular adduction. Destruction of these same fibers results in paralysis of adduction and nystagmus in the abducted eye on attempted lateral gaze. This is similar to the ocular syndrome described clinicopathologically in man, known as internuclear paralysis, or ophthalmoplegia internuclearis, which was first described by Bielschowsky in 1902. Convergence and vestibular function are unaffected.

On the basis of these observations, it appears that the ascending fibers in the median longitudinal fasciculus probably represent the terminal portion of the corticobulbar pathway for horizontal conjugate movements of the eyes. This hypothesis has been supported by observations made on a series of stimulations through the reticular substance, the vestibular nuclei and their emerging fibers.

R IRVINE

### Retina and Optic Nerve

RETINAL DETACHMENT A SERIES OF 78 CASES IN THE MIDDLE EAST FORCE H B STALLARD, Brit M J 2 330 (Sept 9) 1944

This is a report of 78 cases of retinal detachment, in 76 of which operation was performed by a combination of surface diathermy placed around the edges of the tear and a few punctures of penetrating diathermy. The interretinal fluid was sucked into a glass tube applied to the sclera over the diathermy penetration. The patients were all soldiers between the ages of 20 and 47. The survey differs from one of retinal detachment seen in civilian practice in that the incidence of myopia was extremely infrequent, namely, in 3 of 78 cases, and injuries peculiar to war were of course absent in civilian practice.

The cases are divided into five groups: (1) cystic degeneration, 13 cases, (2) chorioretinal degeneration, 21 cases, (3) myopia, 3 cases, (4) trauma (civilian), 23 cases, and (5) trauma

(military), 18 cases. The results of operation were as follows: (1) cystic degeneration, 13 successes and no failures, (2) chorioretinal degeneration, 21 successes and no failures, (3) myopia, 2 successes and 1 failure, (4) trauma (civilian), 20 successes and 3 failures, (5) trauma (military), 10 successes and 6 failures, giving a total of 66 successes and 10 failures. Any recurrence, however slight, of the retinal detachment was recorded as a failure.

The author then describes more fully the factors which serve as a basis for prognosis. The prognosis is favorable in cases of retinal detachment due to cystic degeneration and to chorioretinal degeneration, especially in men of military age. The prognosis is worse for deep detachments than for shallow ones on account of the distance of the retinal tear from the choroid. In this condition the diathermy needles are passed through the sclera and choroid sufficiently long to reach the retina, but not to perforate it (which is the method advocated by Weve, abstracted). Extensive intraocular degeneration, total detachment, high myopia, very low intraocular pressure and detachment in an aphakic eye are bad prognostic signs. Their presence is least favorable in war injuries. This is explained by the presence of additional trauma from a contusion or a penetrating wound.

ARNOLD KNAPP

### Tumors

SECONDARY CARCINOMA IN THE ANTERIOR CHAMBER A J B GOLDSMITH, Brit J Ophth 29 136 (March) 1945

A woman aged 64 had undergone a radical mastectomy for carcinoma of the left breast (confirmed by histologic examination) a year previous to the enucleation of the right eye because of secondary glaucoma, suspected to be due to a carcinoma of the choroid. Histologic study showed that the main mass was on the temporal side, where it extended from near the disk as far forward as the equator. In the sclera the growth extended along the canal of one of the ciliary nerves close to the disk. Cells were present in the ciliary body and the iris. In the angle of the anterior chamber malignant cells had burst through the root of the iris and were proliferating into the anterior chamber, where they formed a plaque lying on the surface of the iris, but not intimately connected with it and deriving no blood supply from it. A few cells lay on the posterior surface of the cornea.

The author supplies the following summary:

"A hitherto undescribed condition is described, in which secondary carcinoma is growing in the anterior chamber after the manner of a tissue culture.

"Attention is drawn to the differences in manner of intra-ocular extension between neuro-epithelial retinal tumours and secondary carcinoma within the eye, and it is suggested that

these are largely the result of the different sites in which the two types of growth originate

"Attention is also briefly drawn to the use made in experimental cancer research of the capacity of the aqueous fluid to act as a tissue culture medium"

W ZENTMAYER

### Vision

AN INTRODUCTION TO BISHOP BERKELEY'S THEORY OF VISION M MURRAY, Brit J Ophth 28:600 (Dec ) 1944

This interesting article does not lend itself to abstraction. The author states and discusses the views of Berkeley, who was an empiricist, the term implying the doctrine that space perception is entirely learnt, as against its being inherited or instinctive. Berkeley has also been described as a tactualist, the term suggests better his doctrine that touch is the space sense *par excellence*, and that sight in its primitive purity is devoid of all space character.

The vista of speculation which the theory opened up formed a background for a controversy which involved many future generations of authorities on visual optics. Two schools of thought exist the empiricists, of which Helmholtz and Wundt are exponents, and the nativists, which include Hering and Muller. The nativists believe in the theory of inheritance.

W ZENTMAYER

SIGHT-SAVING CLASSES N BISHOP HARMAN, Brit M J 1:53 (Jan 13) 1945

The author discusses the technical requirements and potentialities of the school for the partially blind. He gives an extremely inter-

esting historical review of how these sight-saving schools came into being, as he was among one of the earliest persons to become interested in this subject.

In the early work, Harman was much struck by the predominant occurrence of poor sight in girls. Then he found that many of the children in schools for the blind were really not blind, they were highly myopic, could see objects at their own distance very well and mentally were as keen as any other children. This led to the setting up of special classes for the partially blind children, the scheme of work laid down for these classes consisting in (1) oral teaching in groups with the normal children, (2) literary work with the aid of blackboards and chalk and (3) full use of every sort of handicraft which would develop attention, method and skill, with minimum use of the eyes. Special attention was given to such items as proper equipment of the classrooms, exercise books and physical exercises. The most difficult section of the work was manual training; all sewing was prohibited. These classes soon became popular just as they had been popular in the United States, and many of them exist both in London and in the provinces. The important point, the author says, in the training of children with defective vision is proper training so that they use their eyes with intelligence and will be able to carry on with the training after school years.

This article is very interesting, it shows the value of sight-saving classes for the children with partial sight and points out how this training should prevent the loss of sight and save the children from the misery of blindness.

ARNOLD KNAPP

# Society Transactions

EDITED BY DR W L BENEDICT

## NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

THOMAS H JOHNSON, M.D., *Chairman*

WENDELL L HUGHES, *Secretary*

*Regular Meeting, April 16, 1945*

### A Family with Congenitally Subluxated Lenses

DR ROBERT R CHACE

This paper will be published in a later issue of the ARCHIVES

### Marfan's Syndrome with Unusual Complications Report of a Case DR JAMES L McGRAW

This paper was published in the August 1945 issue of the ARCHIVES, page 112

### Ocular Changes Associated with Arachnodactyly. DR RALPH I LLOYD, Brooklyn

This is based on a study of 18 patients under observation over periods of three to thirteen years and some 25 other patients seen over shorter periods. Of the 18 patients, 6 have been operated on, 3 to improve vision and 3 in emergencies. Of the first 3, none was successful. In 1 patient operation was a success but the vision did not improve. Results in the second case were ruined by a hemorrhage into the vitreous and in the third, by a retinal detachment which was operated on with temporary results. Of the second group, 1 patient suffered bilateral dislocation of the lenses into the anterior chamber and the result was highly satisfactory. Another suffered a unilateral dislocation into the chamber, from which the lens was removed without difficulty. Later replacement of iris in the wound, which opened from within, posterior scleral trephine and enucleation were done. The pathologist's report was epithelial invasion of the chamber. The third patient was operated on and reoperated on for retinal detachment without success. Marked changes in position of the lens were seen in 7 cases. Two are mentioned as dislocations into the anterior chamber. Three eyes in 2 patients were dislocated into the vitreous. In 3 cases the dislocation was incomplete but sufficient to uncover the pupil, with improvement in vision in one eye of each patient. These results are discouraging, but one has no way of ascertaining the number of cases of arachnodactyly with normal eyes or satisfactory status quo.

In patients with poor vision there is progressive degeneration with complications, whereas patients with better vision may go along for years without coming into the hands of any one able to recognize the situation. Persons with this condition must be handled with care and judgment, and an effort should be made to discover the safest technic for removal of the lens.

#### DISCUSSION

DR THOMAS H JOHNSON A patient with ectopia lentis presents an important problem. If he is a child, what is to be done? No satisfactory operation has been devised for a subluxated lens. It is known that such lenses do not absorb well after needling. If the lens is removed with a loop, there is danger of subsequent detachment of the retina, regardless of the age of the patient. In the general discussion of this paper, it would be interesting to have opinions as to the type of operation advisable and to hear what complications have occurred in the experience of others.

DR JAMES W SMITH Twenty years ago Ormond and Williams noted that ectopia lentis, iridodonesis and miosis occurred in about 50 per cent of all cases of Marfan's syndrome. Interest of American ophthalmologists in these ocular changes was stimulated by the paper of Dr Lloyd's, read before the American Ophthalmological Society in 1934.

Ectopia lentis occasionally occurs independently of arachnodactyly. Kredbova observed 37 members of a family through four generations, 15 of whom had ectopia, 2 congenital coloboma and 6 myopic changes in the fundus. None of his patients presented typical arachnodactyly. The incidence of ectopia lentis in 75 per cent of the cases of arachnodactyly and analogous anomalies of growth recently reported suggests that the etiologic factors responsible for arachnodactyly are also involved with displacement of the lens.

Dr Lloyd, in his opening statements, properly emphasized the progressive ocular changes seen with this disorder. The small spherophakic lenses are usually dislocated upward. Later they may appear in the anterior chamber and precipitate glaucomatous symptoms. Complete dislocation into the vitreous, with loss of vision, is a common complication. Uveal degeneration and retinal detachment are two serious factors stressed by Dr Lloyd which account for his conservative, nonsurgical approach.

Six of the 18 patients observed by Dr Lloyd had operations. Of the 3 patients for whom operation was optional, 1 had an uncomplicated course but no visual improvement. The second patient had a hemorrhage into the vitreous. The patient referred to me for iridectomy and extraction of the lens of the left eye made an uneventful recovery, with vision limited to 20/60 + 2. Retinal separation occurred thirteen months later, the detached portion being partly replaced by discoidal coagulation. Vision at present, two years later, is 20/80. In 1 of the 3 remaining patients, the lens was removed from the anterior chamber of both eyes for bilateral dislocation, but vision failed nine years later as a result of a pathologic process of the uveal tract. The eye of a second patient was enucleated after removal of the lens from the anterior chamber, and the third patient had an operation for retinal detachment without success. I agree that as long as useful vision is obtained through the aphakic pupillary area with a correcting lens, surgical intervention should not be contemplated.

The operative failures in Dr Lloyd's series make me hesitate to suggest a new surgical approach. I do not believe that these young, structurally defective, globes should be subjected to extraction of the lens with unavoidable loss of vitreous. Needling of the elusive subluxated lens is difficult and inadequate and must be repeated.

Several years ago Dr Arnold Knapp called attention to Bowman's technic, in which two knife needles were used. The patient presented in the adjoining room was first examined in 1934. He was 20 years old and had worn glasses for fifteen years. Minus 15.00 D spheres corrected vision in the right eye to 10/200 and in the left eye to 15/100. The maximum acuity obtained in the right eye with a -30.00 D sphere was 15/100 and that in the left eye with a -21.00 D sphere was 15/50. No gross pathologic process was seen in the right fundus, and the macula was not involved. The lens was luxated nasally. The anterior chamber was shallow, and only moderate iridodonesis was present. The left anterior chamber was deep, and tremor of the iris was pronounced. The temporal equator was displaced posteriorly but remained attached nasally. No details of the fundus were discernible through the small aphakic area.

Three months later the left lens had wandered into the anterior chamber. Needling, attempted with the patient lying face down, failed. Later, with the pupil contracted and the patient in the sitting position, a knife needle was placed in the cornea 3 mm from the temporal limbus, the posterior capsule was engaged, and the lens was forced against the cornea. A generous section was made in the posterior capsule, and cortical clouding began in two days. Two weeks later most of the loose cortex fell into the vitreous and was resorbed. The shrunken lenticular sac

is still seen behind the iris inferiorly. Vision corrected with an aphakic lens is 20/40 +, and the patient, eleven years after discussion, reads Jaeger type 2.

The same operation was performed on the right eye in 1940, when the patient was 26 years of age. Clearing of the lens was slower, and a capsulotomy had to be done. Vision with correction was 20/60, and the patient reads Jaeger type 5 plus.

When Dr Lloyd referred the girl aged 14 to me in 1941, I was anxious to perform a needling of the posterior capsule, but he preferred extraction by spooning. The lens was sharply curved anteriorly and measured 8 mm long and 6 mm wide in the anteroposterior diameter. It weighed only 0.125 Gm, as compared with 0.158 Gm, the average weight for a lens at this age. The patient made an interesting diagnosis of further luxation in the right eye while she was in bed convalescing from my operation for retinal detachment on the left eye. She observed that the aphakic glass prescribed for the left eye after extraction of the lens one year previously afforded remarkable vision in the right eye. She had made this test many times after extraction of the lens, but without result.

I consider the technic which I use in cases of subluxated lenses ideally suited for patients up to the age of 20 years. Glaucoma does not occur as a complication, and the vitreous seems to tolerate young lens cortex. The feature which appeals to me particularly is that the globe is not opened and the vitreous is not lost.

Recent studies of the cause of retinal detachment are pertinent to the present discussion of operations on the lens in children. Dr Knapp's paper on the operative prognosis of congenital cataract (*Operative Prognosis of Congenital Cataract*, ARCH OPHTH 32: 519 [Dec] 1944) was a survey of 400 cases of retinal detachment. In 6, or nearly 16 per cent, of 37 cases of retinal detachment following cataract operations, congenital cataract had been present. Shapland (*Tr Ophth Soc U Kingdom* 54: 176, 1934) reviewed 651 cases of simple detachment of the retina in Moorfield's Eye Hospital, in about 10 per cent of these the patient was aphakic. An analysis of 40 eyes in which needling had been performed in infancy or early childhood for congenital cataract showed that retinal detachment developed in 82.5 per cent. The average interval was twenty-four and six-tenths years, the shortest being six years and the longest forty-one years. My purpose in citing these statistics is to stress the fact that, like ectopia lentis, congenital cataract is a form of defective structural development.

I view with misgiving the practice of subjecting patients with congenital cataract to innumerable needlings, and I should like to ask operations may contribute to, or actually hasten, Dr Lloyd whether he does not feel that repeated

the appearance of retinal separation. It is my own practice to perform a generous dissection of the anterior capsule in young children. If the angle of the chamber should become obstructed, the loose cortex can be irrigated out of the anterior chamber through a small keratome section. In order to avoid subjecting such eyes to repeated trauma, I have on occasion continued the needling through the posterior capsule. As in cases of ectopia lentis, the posterior dissection lessens the possibility of glaucoma developing postoperatively. I should like to ask Dr. Lloyd whether he has any objection to opening the posterior capsule. Will he tell us whether ectopia lentis is found only in cases of Marfan's syndrome?

The Section is indebted to Dr. Lloyd for popularizing a syndrome considered originally to be of interest only to pediatricians and orthopedists. He has directed our attention to the fact that the ocular complications are very common. His youngest patient was 6 years of age. If ophthalmologists follow his suggestion of dilating the pupils in very young children, they may be in a position occasionally to establish the diagnosis before serious skeletal defects are evident clinically.

DR. HERMANN BURIAN, Hanover, N. H. (by invitation). The statement on the program that I am going to discuss Dr. Lloyd's paper is somewhat of a misrepresentation. Even though I have for a long time been interested in the syndrome of arachnodactyly with subluxation of the crystalline lens, I should not presume to discuss Dr. Lloyd's masterly presentation.

I am here only because Dr. Lloyd, when in Hanover last summer, saw a case of arachnodactyly in which I had operated, and he asked me to tell you about it. My comments will be restricted to the report of this case.

R. J. L., a white boy born Dec. 12, 1936, was first seen by me on May 19, 1942, when he was 5½ years of age. There was no relevant family history of ocular disease. The 3 siblings had normal eyes.

The patient had never been seriously ill. He had developed normally and, according to the mother, had shown no signs of mental retardation. However, a diagnosis of congenital heart murmur had been made.

The child had always held objects close to his eyes and had exhibited other signs of poor vision; these had become particularly noticeable in the year prior to examination.

Examination revealed typical signs of arachnodactyly. His arms and legs, particularly his fingers and toes, were very long and thin. The eyes were white and quiet. The irises showed a normal structure but exhibited pronounced iridodonesis. "Spider-web" remnants of the pupillary membrane were seen in the upper part of both pupils, particularly in the right eye. Both crystalline lenses were subluxated downward and

nasally, so that the upper edge of the lens appeared in the lower part of the undilated pupil. The fundi were somewhat depigmented but presented no anomaly. Uncorrected visual acuity was less than 20/400 in each eye; vision could not be improved with glasses. It was difficult, however, to make subjective tests on the rather unresponsive patient. A diagnosis of Marfan's syndrome was made, and hospitalization was advised.

In June 1942 the patient was admitted to the hospital for examination and treatment. Physical examination revealed no noteworthy anomaly aside from the arachnodactyly. The heart was normal except for a rapid rate. There was reduplication of the second sound at the apex, which was heard better medially. The pulsations of the dorsalis pedis artery were weak, but those of the popliteal artery were normal. The Vollmer patch test for tuberculosis gave a negative response. Complete blood counts, serologic tests and urinalysis gave normal results. Roentgenograms of the chest, skull and upper extremities revealed nothing abnormal. An electrocardiogram was essentially normal.

On June 25 a dissection of the right lens was attempted. Two dissection knives were introduced into the anterior chamber, one from each side, at 4 and 8 o'clock respectively. The lens was held with one knife and the dissection performed with the other. No clouding of the lens was obtained, and on June 30 extraction of the right lens through a keratome incision was attempted. Grasping of the lens with the capsule forceps did not succeed, and the lens was delivered by a loop, with considerable loss of vitreous. The condition of the eye quieted down, but the pupil was distorted upward, and on October 1 an iridotomy was performed by introducing a dissection knife into the anterior chamber near the limbus at 12 o'clock. A section through the iris was made in the vertical meridian, and a good opening in the iris was obtained.

The boy was readmitted in January 1943. He had a slight elevation of temperature, and operation was postponed for a few days. There were enlarged anterior cervical glands. One observer thought that there was a soft, late systolic murmur at the apex, and another observer heard a diastolic murmur at the apex. But the next day, with a slower heart rate, this resolved itself into a reduplication of the heart sounds, as noted on the first admission. For two days shortly after his operation he again had a rather high fever, and it was thought at the time that he had grip, but the lungs were clear and there were only a cough, enlarged cervical glands and reddening of the throat. Blood counts and urinalysis again gave normal results.

On Feb. 5, 1943 the left lens was removed. The anterior chamber was opened with a keratome at the upper limbus. Pressure was exerted on the lower limbus and the lens grasped with



intracapsular forceps and lifted into the anterior chamber. It was removed from the chamber by combined pressure and traction. The lens proved to be small and globular. No vitreous was lost.

In spite of the smoothness of the operative procedure and the application of physostigmine, the upper part of the iris became inverted, and the pupil, accordingly, was distorted to such an extent that it was covered by the upper lid.

On July 6, 1943 an iridotomy was performed on the left eye. The discission knife was inserted through the upper limbus and the iris sectioned in the vertical meridian with sawing movements. The postoperative course was uneventful.

The patient was followed through 1943 and 1944, when he was last seen, on Nov 13, 1944, the condition was as follows. Both eyes were white and quiet. The pupils were triangular, the right one being smaller than the left. The pupillary areas were black, and the fundi appeared normal. The best vision was obtained with a correction of  $+10.00$  D sph  $\subset +2.00$  D cyl, axis 180, which gave visual acuity of 20/60  $+2$  in the right eye, 20/60 in the left eye and 20/50  $+2$  binocularly. The keratometric readings showed astigmatism of  $-6.50$  D at axis 93 in the right eye and  $-6.00$  D at axis 100 or 110 in the left eye.

DR CLYDE E. McDANNALD: May I ask Dr. Lloyd whether there are any statistics relating to hereditary transmission? I have not heard of any.

DR WILLIS S. KNIGHTON: I should like to report the case of a man 27 years of age in which there were features which differed a little from those reported tonight. The patient was well built but had all the characteristics of arachnodactyly. The interesting observation on refraction was that the lenses were dislocated downward, so that the upper border was exactly in the center of the pupil in each eye, and his vision could be improved by correction with either plus or minus spheres. He was very uncomfortable with minus spheres, and vision was only 20/70 in each eye, but with plus spheres vision was 20/40 in the right eye and 20/20 in the left eye. My colleagues and I had planned to do an intracapsular extraction with iridectomy, but the response of the pupil to the mydriatic was so great that the iris was just a narrow band, the lens was therefore removed through a round pupil. As soon as the section was made, the lens floated up toward the cornea and was delivered with a loop alone, almost no traction was necessary, and no counterpressure was made. There was no loss or presentation of vitreous. Convalescence was uncomplicated, and his vision was 20/20— with correction. The astonishing thing was that with plus spheres for his right, completely aphakic, eye and for his left, half aphakic, eye he had comfortable binoc-

ular vision. Dr. Lloyd suggested that we remove the lens of the left eye. The patient did not return to the clinic for two years, although he had been doing hard manual labor, there was no further dislocation of the lens in the left eye. Extraction of the lens in the left eye was performed, with the same result. He was last seen four years after the first operation and two years after the second operation. At that time he had 20/20— vision in each eye, with good binocular vision.

DR RALPH I. LLOYD, Brooklyn: Certainly, all luxations of the lens are not due to arachnodactyly, but all congenital bilateral luxations should be considered as associated with arachnodactyly unless proved otherwise. When a case of bilateral luxation is found, the family tree should be thoroughly studied to find a transmitter of this, usually dominant, trait. The parent may have normal bony structure and mild luxation with good vision, or he may have normal eyes and the characteristic changes of the bones. Persons with either type may have offspring with typical arachnodactyly. When operation to improve vision must be done, younger patients seem to fare better than adolescents and adolescents better than adults. As a rule the lens can be easily removed without using the spoon, for such a lens is lighter and smaller than the normal lens. It will float up into the wound if an iridectomy is done. The best operation is the one that disturbs the eye the least, and probably needling is safer. I have seen Dr. Smith do the operation he has described here, although it is slow and may have to be done again, the results are very good. However, I am not committed absolutely to any one procedure, and I prefer to play out the hand as the cards may fall. It is plain from what has been said that cases of this syndrome are not a favorable group for any operation.

#### Traumatic Staining of the Conjunctiva with Indelible Lead: Report of a Case. DR HAROLD WASS

This case is presented because of the bizarre clinical appearance and because of the excellent result obtained with subconjunctival irrigation with saline solution. The patient was seen in the emergency clinic of the New York Eye and Ear Infirmary, in the service of Dr. Willis Knighton, one-half hour after the conjunctiva was lacerated with the point of an indelible pencil. Pieces were removed from under the conjunctiva with forceps, and the cul-de-sac was irrigated freely with warm saline solution. Many pieces and grains of lead remained under the conjunctiva, and the whole globe was stained a brilliant violet.

Irrigation of the subconjunctival space with saline solution and closure of the conjunctival wound with black silk sutures were done in the surgical service, this treatment resulted in complete fading of the stain in forty-eight hours.



In addition to the mechanical cleansing of the subconjunctival space the black silk sutures may have stimulated phagocytosis by acting as an additional foreign body. However, the same indelible lead was inserted below the conjunctiva in 1 rabbit eye and into the vitreous cavity of another. Enucleation was performed two weeks later, and microscopic examination of the slides showed no cellular reaction in either globe and nothing resembling phagocytosis. The indelible lead remained relatively inert in the rabbit eye.

The sections of the rabbit eyes were prepared by Dr E. B. Buichell, of the Eno Laboratory of the New York Eye and Ear Infirmary, and the Kodachromes were made by the department of photography. None of the bleaches used by the personnel of the manufacturing companies are suitable for ophthalmic use.

#### DISCUSSION

DR WILLIS S. KNIGHTON: A point of practical importance is the fact, according to Dr Sitchevska, that self-inflicted wounds of this sort were rather common in the Russian army. In view of the clinical course in this case, however, the method does not seem a very practical means of escaping military duty, because the dye disappears so rapidly. However, the picture is so striking at first, when the color is present, that I can see how a draft board, or similar body, would give a man temporary leave at least.

#### Response of Chronic Simple Glaucoma to Treatment with Cyclodiathermy Puncture

DR FREDERICK W. STOCKER, Durham, N. C.

This paper was published in full in the September issue of the ARCHIVES, page 181.

#### DISCUSSION

DR ARNOLD KNAPP: Dr Stocker has undoubtedly covered this point in his admirable presentation, but I should like to ask him to tell us again whether he has ever seen any damage done to an eye by this operation. It has seemed to me that it is difficult to gauge just the number of diathermy punctures required in a particular case and that it is easy to do too much.

The statement that notwithstanding atrophy of a part of the ciliary body eyes with this condition do not show any subsequent deterioration is particularly interesting.

I should like to ask Dr Stocker whether he has tried this operation in a case of secondary glaucoma following thrombosis of the central retinal vein.

DR G. BONACCOLTO: Years ago I was interested in Dr Lagrange's work on *colmatage* in cases of detachment of the retina. This consisted in electrocauterization of the sclera, first at the inferior and, a few weeks later, at the superior limbal region. He had observed intraocular hypotension in eyes with detachment of the retina. With this procedure he produced intra-

ocular hypertension, which, in his opinion, should help to push the retina into place.

I performed this operation in a few cases of detachment of the retina during the period from 1928 to 1932. I obtained moderate hypertension, which lasted as long as I was able to follow the patients.

Will Dr Stocker explain the reason for the difference in the results obtained by him and by Lagrange when they used similar procedures?

DR KAUFMAN SCHLIVK: It is a rare opportunity to listen to a paper describing the results of a new operation covering 100 cases or more. Many years ago I performed this operation in a number of cases of absolute glaucoma, and in the past two and a half years I have used the same method in 4 cases of glaucoma with vision, in all instances the results were satisfactory. One patient was a Negro woman who had had several operations for glaucoma on her left eye, and the eye was blind. The other eye had chronic simple glaucoma with good vision and rather poor fields, the operation recommended by Dr Stocker was done, and the result was excellent. The other 3 patients had had several operations, without benefit, this operation controlled the tension, and vision was retained.

DR WILLIS S. KNIGHTON: As I understand it, glaucoma can be caused either by obstruction to the outflow of the aqueous or by an increase in the inflow of the aqueous. This operation is designed apparently to reduce the inflow of the aqueous. I should like to ask Dr Stocker whether he would try to reduce the production of aqueous almost to the vanishing point in cases in which the obstruction to the outflow is nearly complete.

DR FREDERICK W. STOCKER, Durham, N. C.: To answer Dr Knapp first. One must keep distinct experience in cases of chronic simple glaucoma and experience in cases of secondary glaucoma in which this operation has already been performed a number of times or in which two or three other operations have been done without success. I used to employ considerably stronger current and larger needles in these cases of long standing, and I believe that with this technic I should not have dared to approach the good eyes with chronic simple glaucoma. But by using a very short needle and very little current, as I did in this series of cases of chronic glaucoma in which no other operation had been employed, I have not observed any permanent damage to the eye. I have called this report a preliminary one because I may have to watch the patients for a longer time. However, I think that if after eight or ten months one cannot see any appreciable damage to the eye, one is justified in doing more operations of this kind.

Glaucoma associated with thrombosis of the central retinal vein is in another category, and I have treated several patients with this type

In one such patient the eye was cured of its glaucoma for almost two years after the first thrombosis occurred and was painless, and the vitreous had cleared up to such a degree that I could see the strange fundus picture of healed thrombosis of the central vein. So the eye had completely recovered, but two years later the patient had a tremendous hemorrhage in the vitreous, which led to enucleation. I think one is justified in using this method in cases of thrombosis of the retinal vein causing glaucoma, for I do not know of any other method which will give such good results. I believe that with a secondary type of glaucoma cyclodiathermy puncture is of great value, and chronic inflammatory and painful eyes have a remarkable tendency to become painless. Even if the tension is not quite reduced to normal, the patient does not suffer any more.

The hypotension associated with detached retina, so far as I could understand from Dr. Bonaccolto, was treated with the application of electrocautery, which is a different type of treatment than cyclodiathermy puncture. With the diathermy cautery one does not produce so much inflammation on the surface of the sclera, as it is at the point of the needle that the most intensive coagulating action is to be expected. I cannot explain offhand why the electrocautery should produce permanent hypertension. As I said, my associates and I observed temporary hypertension for several days in a few

cases, but, as I also demonstrated, this does not mean anything in the final outcome, for those cases in which there was a relatively high tension after the operation were not among those in which tension was high at the end.

I am encouraged to hear from Dr. Schlivek that in 1 case of simple chronic glaucoma in which no treatment had previously been employed this operation had given satisfactory results in the hands of some one else.

In answer to Dr. Knight's question about the theory of inflow and outflow of aqueous, I had to limit myself to the simplest principles in order to demonstrate what is involved if one wishes to reduce the tension by achieving a decrease in inflow of liquid. In cases of simple chronic glaucoma, with a tension of about 30 or 35 mm. of mercury, one would not expect complete blockage of the outflow. I do not know how much of the ciliary body would have to be destroyed when complete obstruction is present. In cases of secondary glaucoma, for instance, with thrombosis of the central vein, in which the iris is pushed forward and is adherent to the posterior surface of the cornea, one might have almost complete blockage of the angle of the chamber. But it is known that there are other possible paths of outflow in the eye. The iris and the choroid can absorb fluid, and there is a flow of fluid through the vitreous along the canal of Cloquet. Therefore it is almost impossible to determine when the outflow would be 100 per cent blocked.

## Book Reviews

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**The Psychology of Seeing** By Herman F Brandt, Ph D Price \$3.75 Pp 240 New York Philosophical Library, Inc., 1945

This small volume is misnamed, because it is not a consideration of the psychology of seeing but a study of the results of behavior patterns obtained by means of ocular photography.

The author has invented a camera for recording eye movements. In many ways it is similar to the score or more of eye movement cameras which preceded it and which culminated in the ophthalmograph with which ophthalmologists are familiar. It has the advantage that the movements of the eyes in observing a double page magazine layout (such as *Saturday Evening Post* or *Life*) can be photographed on a single stationary film and the progress of the eye movements studied from a projection of the photograph back on to the original copy.

Of the eight parts of the book, the first is an elementary discussion of psychology, the second a description of the camera and the third a demon-

stration of basic eye movements. The fourth part is devoted to advertising as evaluated by means of the author's camera. Part V is the most scientific chapter of the book, in which various problems of learning are studied by means of photographs of eye movements. It is largely from this chapter that the ophthalmologist would derive any profit. Part VI is a discussion of art as judged by camera studies of eye movements, part VII discusses factors involved in ocular patterns, and in the final chapter the author projects future studies to be carried out, using his instrument and technics, in such diverse fields as crime detection and talking books.

The book is largely written for the advertising industrialist, who wants to get his message, pictorial or printed, in a preferred position and to grasp and hold the attention of readers against the clamor of competitors. It has little to do with ophthalmology except for the parts relating to reading and learning difficulties. These are discussed diagnostically, with few if any therapeutic suggestions.

LEGRAND H. HARDY

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Bombay 12 Time First Friday of every month

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Place Edinburgh and Glasgow, in rotation

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stitucion, Santa Fe  
Place Rosario Time Last Saturday of every month,  
April to November All correspondence should be  
addressed to the President

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Secretary Dr R J Masters, 23 E Ohio St, Indian-  
apolis  
In compliance with the request of the Office of Defense  
Transportation and in the interest of the national war  
effort a meeting will not be held in 1945

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTO-  
LARYNGOLOGY, SECTION ON OPHTHALMOLOGY

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Executive Secretary-Treasurer Dr William L Bene-  
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President Dr N Zwaifler, 46 Wilbur Ave, Newark  
Secretary Dr William F Keim Jr, 25 Roseville Ave,  
Newark  
Place 91 Lincoln Park South, Newark Time 8 45  
p m, second Monday of each month, October to May

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OTOLARYNGOLOGY

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Secretary-Treasurer Dr Merrill J King, 264 Beacon  
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Place Massachusetts Eye and Ear Infirmary, 243  
Charles St, Boston Time 8 p m, third Tuesday of  
each month from November to April, inclusive

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Bldg, Seattle 1  
Place Seattle or Tacoma, Wash Time Third Tues-  
day of each month except June, July and August

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THROAT SOCIETY

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Time Third Tuesday of each month from October  
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Secretary-Treasurer Dr Harold H Heuser, 207  
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Place Saginaw or Bay City, Mich Time Second  
Tuesday of each month, except July, August and  
September

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Secretary-Treasurer Dr Kenneth Lowe, 25 W Mich-  
igan Ave, Battle Creek  
Time Last Thursday of September, October, Novem-  
ber, March, April and May

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## COLORADO OPHTHALMOLOGICAL SOCIETY

President Dr C A Ringle, 912-9th Ave, Greeley  
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 Denver  
 Place University Club, Denver Time 7 30 p m,  
 third Saturday of each month, October to May, in-  
 clusive

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON  
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OTOLARYNGOLOGY

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 Paul 2  
 Secretary Dr William A Kennedy, 372 St Peter St,  
 St Paul 2  
 Time Second Friday of each month from October to  
 May

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President Dr Paul Neely, 1020 S W Taylor St,  
 Portland  
 Secretary-Treasurer Dr Lewis Jordon, 1020 S W  
 Taylor St, Portland  
 Place Good Samaritan Hospital, Portland Time  
 Third Tuesday of each month

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr Lewis T Buckman, 83 S Franklin St,  
 Wilkes-Barre  
 Secretary Pro Tem Dr Paul C Craig, 232 N 5th  
 St, Reading  
 Time Last week in April

RHODE ISLAND OPHTHALMOLOGICAL AND  
OTOLOGICAL SOCIETY

Acting President Dr N Darrell Harvey, 112 Water-  
 man St, Providence  
 Secretary-Treasurer Dr Linley C Happ, 124 Water-  
 man St, Providence  
 Place Rhode Island Medical Society, Library, Provi-  
 dence Time 8 30 p m, second Thursday in  
 October, December, February and April

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Secretary Dr M K McCullough, 1717 Pacific Ave, Dallas

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President Dr E B Fairbanks, 315 Medical Arts Bldg, Salt Lake City  
Secretary-Treasurer Dr Dean Spear, 516 Boston Bldg, Salt Lake City  
Place University Club, Salt Lake City Time 7 00 p m, third Monday of each month

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Secretary-Treasurer Dr Meade Edmunds, 34 Franklin St, Petersburg

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OTOLARYNGOLOGY**

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Secretary-Treasurer Dr V C Malloy, 2d National Bank Bldg, Akron, Ohio  
Time First Monday in January, March, May and November

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President Dr B M Cline, 153 Peachtree St N E, Atlanta, Ga  
Acting Secretary Dr A V Hallum, 478 Peachtree St N E, Atlanta, Ga  
Place Grady Hospital Time 6 00 p m, fourth Monday of each month, from October to May

**BALTIMORE MEDICAL SOCIETY, SECTION ON  
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Chairman Dr Ernst Bodenheimer, 1212 Eutaw Pl, Baltimore  
Secretary Dr Thomas R O'Rourke, 104 W Madison St, Baltimore  
Place Medical and Chirurgical Faculty, 1211 Cathedral St Time 8 30 p m, fourth Thursday of each month from October to March

**BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB**

President Each member, in alphabetical order  
Secretary Dr Luther E Wilson, 919 Woodward Bldg, Birmingham, Ala  
Place Tutwiler Hotel Time 6 30 p m, second Tuesday of each month, September to May, inclusive

**BROOKLYN OPHTHALMOLOGICAL SOCIETY**

President Dr Michael J Buonaguro, 589 Lorimer St, Brooklyn 11  
Secretary-Treasurer Dr Louis Freemark, 256 Rochester Ave, Brooklyn 13  
Place Kings County Medical Society Bldg, 1313 Bedford Ave Time Third Thursday in February, April, May, October and December

**BUFFALO OPHTHALMOLOGIC CLUB**

President Dr William H Howard, 389 Linwood Ave, Buffalo 9  
Secretary-Treasurer Dr Sheldon B Freeman, 196 Linwood Ave, Buffalo 9  
Time Second Thursday of each month from October to May

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OTOLARYNGOLOGY**

President Each member, in alphabetical order  
Secretary Dr Douglas Chamberlain, Chattanooga Bank Bldg, Chattanooga, Tenn  
Place Mountain City Club Time Second Thursday of each month from September to May

**CHICAGO OPHTHALMOLOGICAL SOCIETY**

President Dr Samuel J Meyer, 58 E Washington St, Chicago 2  
Secretary Dr W A. Mann, 30 N Michigan Ave, Chicago 2  
Place Continental Hotel, 505 N Michigan Ave Time Third Monday of each month from October to May

**CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY  
STAFF**

Chairman Dr D T Vail, 441 Vine St, Cincinnati  
Secretary Dr A A Levin, 441 Vine St, Cincinnati  
Place Cincinnati General Hospital Time 7 45 p m, third Friday of each month except June, July and August

**CLEVELAND OPHTHALMOLOGICAL CLUB**

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Secretary Dr H H Wygand, Guardian Bldg, Cleveland  
Time Second Tuesday in October, December, February and April

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Chairman Dr W S Reese, 1901 Walnut St, Philadelphia  
Clerk Dr. George F J Kelly, 37 S 20th St, Philadelphia  
Time Third Thursday of every month from October to April, inclusive

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Chairman Dr Erwin W Troutman, 21 E State St, Columbus, Ohio  
 Secretary-Treasurer Dr T Rees Williams, 380 E Town St, Columbus 15, Ohio  
 Place University Club Time 6 15 p m, first Monday of each month, from October to May, inclusive

## CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr C B Collins, 704 Medical Professional Bldg, Corpus Christi, Texas  
 Secretary Dr L W O Janssen, 710 Medical Professional Bldg, Corpus Christi, Texas  
 Time 6 30 p m, third Tuesday of each month from October to May

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President Dr Ruby K. Daniel, Medical Arts Bldg, Dallas 1, Texas  
 Secretary Dr Tom Barr, Medical Arts Bldg, Dallas 1, Texas  
 Place Dallas Athletic Club Time 6 30 p m, first Tuesday of each month from October to June The November, January and March meetings are devoted to clinical work

## DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr H C Schmitz, 604 Locust St, Des Moines, Iowa  
 Secretary-Treasurer Dr Byron M Merkel, 604 Locust St, Des Moines, Iowa  
 Time 7 45 p m, third Monday of every month from September to May

## DETROIT OPHTHALMOLOGICAL CLUB

Chairman Members rotate alphabetically  
 Secretary Dr Wesley G Reid, 667 Fisher Bldg, Detroit 2  
 Place Club rooms of Wayne County Medical Society  
 Time First Monday of each month, November to April, inclusive

## DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Raymond S Goux, 545 David Whitney Bldg, Detroit 26  
 Secretary Dr Arthur Hale, 1609 Eaton Tower, Detroit 26  
 Place Club rooms of Wayne County Medical Society  
 Time 6 30 p m, third Thursday of each month from November to April, inclusive

## EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President Appointed at each meeting  
 Secretary-Treasurer Dr Joseph L Holohan, 330 State St., Albany  
 Time Third Wednesday in October, November, March, April, May and June

## FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Rex Howard, 602 W 10th St, Fort Worth, Texas  
 Secretary-Treasurer Dr R H Gough, Medical Arts Bldg, Fort Worth, Texas  
 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each month except July and August

## HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SECTION

President Dr Lyle J Logue, 1304 Walker Ave, Houston, Texas  
 Secretary Dr John T Stough, 803 Medical Arts Bldg, Houston, Texas  
 Place Medical Arts Bldg, Harris County Medical Society Rooms Time 8 p m, second Thursday of each month from September to June

## INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr Myron Harding, 23 E Ohio St, Indianapolis  
 Secretary Dr Kenneth L Craft, 23 E Ohio St, Indianapolis  
 Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each month from November to May

## KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo  
 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo  
 Time Third Thursday of each month from October to June The November, January and March meetings are devoted to clinical work

## LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Francis Carl Hertzog, 117 E 8th St, Long Beach, Calif  
 Secretary-Treasurer Dr Robert G Thornburgh, 117 E 8th St, Long Beach, Calif  
 Place Seaside Hospital Time Last Wednesday of each month from October to May

## LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Orrie E Ghrist, 210 N Central Ave, Glendale, Calif  
 Secretary-Treasurer Dr K C Brandenburg, 110 Pine Ave, Long Beach 2, Calif  
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time 6 30 p m, fourth Monday of each month from September to May, inclusive

## LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky  
 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky  
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

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THROAT SOCIETY

Chairman Each member in alphabetical order  
Secretary Dr James J Monohan, 31 S Jardin St,  
Shenandoah, Pa

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SECTION OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

Chairman Dr P S Constantinople, 1835 I St N W,  
Washington  
Secretary Dr Frazier Williams, 1801 I St N W,  
Washington  
Place 1718 M St N W Time 8 p m, third Friday  
of each month from October to April, inclusive

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

Chairman Each member, in alphabetical order  
Secretary Dr Sam H Sanders, 1089 Madison Ave,  
Memphis, Tenn  
Place Eye Clinic of Memphis Eye, Ear, Nose and  
Throat Hospital Time 8 p m, second Tuesday of  
each month from September to May

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Ralph T Rank, 238 W Wisconsin Ave,  
Milwaukee  
Secretary-Treasurer Dr Frank G Treskow, 411 E  
Mason St, Milwaukee 2  
Place University Club Time 6 30 p m, fourth  
Tuesday of each month from October to May

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Chairman Dr H V Dutrow, 1040 Fidelity Medical  
Bldg, Dayton, Ohio  
Secretary-Treasurer Dr Maitland D Place, 981 Rei-  
bold Bldg, Dayton, Ohio  
Place Van Cleve Hotel Time 6 30 p m, first Tues-  
day of each month from October to June, inclusive

MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr J Rosenbaum, 1396 Ste Catherine St  
W, Montreal, Canada  
Secretary Dr L Tessier, 1230 St Joseph Blvd E,  
Montreal, Canada  
Time Second Thursday of October, December, Febru-  
ary and April

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Chairman Dr M M Cullom, 700 Church St, Nash-  
ville, Tenn.  
Secretary Dr R. E Sullivan, 432 Doctors Bldg,  
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Place James Robertson Hotel Time 6 30 p m, third  
Monday of each month from October to May

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Place Louisiana State University Medical Bldg  
Time 8 p m, second Tuesday of each month from  
October to May

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Secretary Dr Truman L Boyes, 654 Madison Ave,  
New York  
Time 8 30 p m, third Monday of every month from  
October to May, inclusive

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OPHTHALMOLOGY

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Secretary Dr Benjamin Esterman, 983 Park Ave,  
New York 28  
Place New York Academy of Medicine, 2 E 103d St  
Time 8 p m, first Monday of each month from  
October to May, inclusive

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AND OTOLARYNGOLOGY

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Oklahoma City  
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Secretary-Treasurer Dr W Howard Morrison, 1500  
Medical Arts Bldg, Omaha 2  
Place Omaha Club, 20th and Douglas Sts, Omaha  
Time 6 p m dinner, 7 p m program, third Wednes-  
day of each month from October to May

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 Secretary Dr T E Sanders, 508 N Grand Blvd, St Louis 3  
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 Time 7 p m, second Tuesday of each month from October to May

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Chairman Dr Roy H Parkinson, 870 Market St, San Francisco  
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 Place Society's Bldg, 2180 Washington St, San Francisco Time Fourth Tuesday of every month except June, July and December

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President Dr David C Swearingen, Slattery Bldg, Shreveport, La  
 Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La  
 Place Shreveport Charity Hospital Time 7 30 p m,  
 first Monday of every month except July, August and September

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President Dr Clarence A Veasey Sr, 421 W Riverside Ave, Spokane, Wash  
 Secretary Dr Clarence A Veasey, 421 W Riverside Ave, Spokane, Wash  
 Place Spokane Medical Library Time 8 p m, fourth  
 Tuesday of each month except June, July and August

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 First Monday of each month, November to April

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 Place Office of chairman Time Last Tuesday of  
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## EVALUATION OF STEREOPSIS

A COMPARISON OF THE HOWARD-DOLMAN AND THE VERHOEFF TEST

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ANDOVER, MASS

Increasing use of visual tests in the field of personnel selection,<sup>1</sup> special military needs and the rapid expansion of aviation have stimulated interest in technics which measure stereopsis. For several years the Howard-Dolman test of stereopsis<sup>2</sup> (not to be confused with the original Howard test<sup>3</sup>) has been used extensively, and more recently Verhoeff<sup>4</sup> has described another method. Verhoeff's test evaluates the acuity of stereopsis by means of a simple device which causes the estimate of relative depth to be based on binocular parallax, eliminates eye-hand coordination and difference in image size as aids in forming judgments and permits little opportunity (1 chance in 65,000) for passing the test by guessing.<sup>4</sup> The results obtained when a group of adolescents was given both these tests are discussed in this report.

### METHOD

The entire student population of a boys' preparatory school was given a thorough ophthalmic examination,<sup>5</sup> and from this group of 720 boys 186 who fulfilled the following requirements were selected for the tests of stereoscopic ability: normal color vision, a normal external ocular condition, normal fundi, normal pupils, a visual acuity of 20/20 in each eye, less than 1.5 D of hyperopia, less than 1.25 prism diopters of hyperphoria, less than 4 prism diopters of exophoria and less

than 6 prism diopters of esophoria at 20 feet (6 meters), less than 6 prism diopters of esophoria and less than 8 prism diopters of exophoria at 16 inches (40 cm) and less than 1 D of astigmatism. Hyperphoria was measured with the Maddox rod, esophoria and exophoria at 20 feet with the Maddox rod and the cover test, and esophoria and exophoria at 16 inches by von Graefe's prism test and the cover test.

Each of these 186 boys was subsequently given the Howard-Dolman test according to the method commonly employed<sup>2</sup>; three successive readings were taken and recorded. The Verhoeff test<sup>4</sup> consists of three vertical black paper strips viewed against a translucent background. The subject is asked to state which of the strips is nearest, or farthest from, him. The test

TABLE 1—*Distribution of Averages of the First Three Trial Settings of the Howard-Dolman Apparatus for 186 Subjects*

Average Setting (Howard Dolman), Mm	Number of Subjects
0 4	34
5 9	63
10 14	40
15 19	20
20 24	9
25 29	7
30 34	3
35 39	3
40 44	0
45 49	3
50 54	0
55 59	0
60 64	2
65 69	2
Total	186

device is first held at a distance of 210 cm from the subject and then moved closer to him until the distance at which his response is correct can be determined. Eight different relative positions of the strips can be obtained, and the distance at which the subject makes the correct response to all these positions is recorded.

### RESULTS

In table 1 is shown the distribution of the averages of the first three trial settings of the Howard-Dolman apparatus, about 85 per cent of the subjects had an average score of less than

1 Kuhn, H S. Significance of Visual Defects in War Production Effort, J A M A 123 1085-1087 (Dec 25) 1943

2 Armstrong, H G. Principles and Practice of Aviation Medicine, Baltimore, Williams & Wilkins Company, 1939, p 77

3 Howard, H J. A Test for the Judgment of Distance, Tr Am Ophth Soc 17 195, 1919

4 Verhoeff, F H. Quantitative Test for Acuity and Reliability of Binocular Stereopsis, Arch Ophth 28 1000-1014 (Dec) 1942

5 Sloane, A E, and Gallagher, J R. A Summary of Findings at the Eye Examination of Preparatory School Boys, Am J Ophth 26 1076-1083 (Oct) 1943



20 mm, and about 5 per cent had average scores greater than 34 mm

The distribution of the averages of the eight ratings on the Verhoeff test is given in table 2

TABLE 2—Distribution of Averages for 186 Subjects of Distances at Which the Eight Correct Responses to the Verhoeff Test Were Made

Average Rating (Verhoeff), Cm	Number of Subjects
50	1
60	0
70	7
80	1
90	1
100	3
110	3
120	7
130	11
140	14
150	11
160	28
170	34
180	28
190	17
200 or more	22
Total	186

About 82 per cent of the group made correct responses at an average distance of 140 cm or more, and about 5 per cent were unable to give correct responses unless the test object was 90 cm or less away. The correlation between the averages of the three Howard-Dolman settings and the averages of the first three Verhoeff ratings was only 0.438.

In evaluating any testing method it is proper to determine how much variation exists between each one of a series of trials. Coefficients of self reliability between each of the first three Verhoeff ratings and between each of the three ratings on the Howard-Dolman test are listed in table 3. A considerably higher coefficient of

TABLE 3—Coefficients of Self Reliability Between First and Second, Second and Third and First and Third Howard-Dolman Settings and Between Similarly Related Verhoeff Ratings

	Howard Dolman	Verhoeff
r <sub>12</sub>	0.280	0.646
r <sub>23</sub>	0.338	0.758
r <sub>13</sub>	0.277	0.520
Average	0.298	0.641

self reliability was found between the first and the second (r<sub>12</sub>), the second and the third (r<sub>23</sub>) and the first and the third (r<sub>13</sub>) Verhoeff ratings than between any two of the Howard-Dolman settings. This difference in degree of self reliability between the two methods suggests that the Howard-Dolman test involves more than pure stereopsis.

The translation of both the Howard-Dolman settings and the Verhoeff ratings into terms of absolute deviations in seconds of arc<sup>6</sup> permits a

further comparison of the results of one test with those of the other. The distribution of the adjusted readings obtained in each of the tests is given in table 4, the much greater range of

TABLE 4—Distribution of Averages of Three Ratings of Both the Verhoeff and the Howard-Dolman Test When These are Expressed in Terms of Absolute Deviations in Seconds of Arc

Verhoeff Test				Howard Dolman	
Average (Seconds of Arc)	Number of Subjects	Average Response	Number of Subjects	Average (Seconds of Arc)	Number of Subjects
3.8-3.9	16	24.0	0	0.1-0.9	42
4.0	36	25.0	0	1.0	65
5.0	35	26.0	0	2.0	37
6.0	32	27.0	0	3.0	17
7.0	16	28.0	1	4.0	10
8.0	8	29.0	0	5.0	4
9.0	10	30.0	0	6.0	2
10.0	5	31.0	0	7.0	2
11.0	4	32.0	0	8.0	3
12.0	3	33.0	0	9.0	0
13.0	4	34.0	0	10.0	1
14.0	3	35.0	0	11.0	2
15.0	0	36.0	0	12.0	1
16.0	1	37.0	2		
17.0	1	38.0	2		186
18.0	1	46.0	2		
19.0	0				
20.0	0		186		
21.0	1				
22.0	1				
23.0	2				

TABLE 5—Verhoeff and Howard-Dolman Ratings, Expressed in Terms of Absolute Deviations in Seconds of Arc, for Subjects Who Made the Seven Lowest Average Scores on Each Test

Verhoeff Rating in Seconds of Arc	Subject	Howard Dolman Rating in Seconds of Arc	Howard Dolman Rating in Seconds of Arc	Subject	Verhoeff Rating in Seconds of Arc
28	W. T.	5.62	8	T. McG.	46.0
37	D. D.	7.26	8	J. M.	5.5
37	D. T.	5.37	8	J. P.	17.7
38	J. H.	3.04	12	R. T.	23.4
38	J. A.	3.90	11	G. J.	7.0
46	P. W.	3.16	11	M. W.	10.2
46	T. McG.	8.0	10	J. R.	11.6

6 Translation of Verhoeff readings into absolute deviations in seconds of arc was made as shown in the following computation:

Verhoeff reading, 150 cm

2.5 mm displacement (depth between strips at the front and those at the back of the test device)

3.2 cm (one-half the average interpupillary distance)

$$\tan Q = \frac{150 \text{ cm}}{3.2 \text{ cm}} \qquad Q = 88^\circ 46' 40.35''$$

$$\tan Q_1 = \frac{150.25 \text{ cm}}{3.2 \text{ cm}} \qquad Q_1 = 88^\circ 46' 47.67''$$

$$Q_1 - Q = 7.32''$$

Verhoeff reading of 150 cm = 7.32 seconds of arc

However, in the translation of Howard-Dolman settings, the calculation was made using 10.92 mm as equal to 2 seconds of arc. Because of the great distance from the subject's eyes, the slight variation in the angle subtended was disregarded.

ratings in the Verhoeff test suggests that this test may detect persons with poor stereopsis whose responses on the Howard-Dolman test might not be considered abnormal

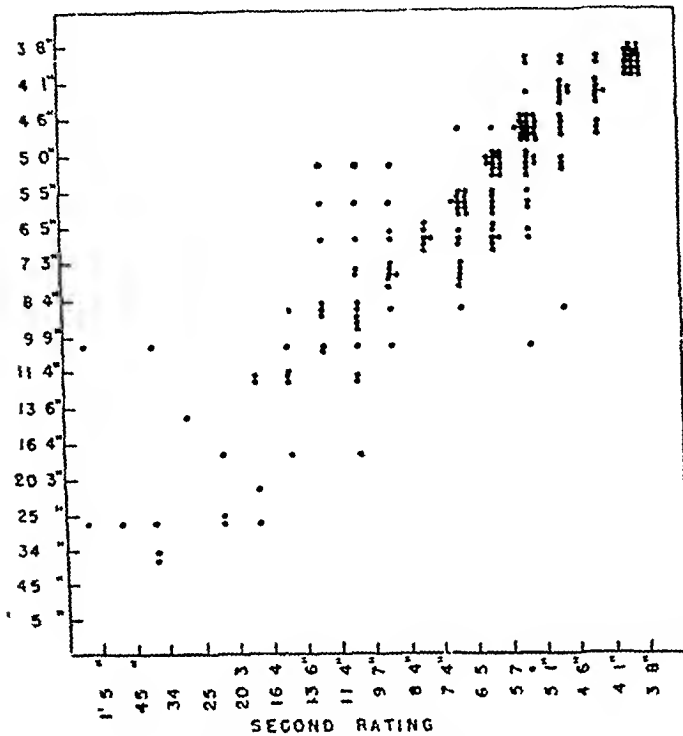


Fig 1—The second and the third Verhoeff rating, expressed in terms of absolute deviation in seconds of arc, plotted against each other to indicate their degree of correlation

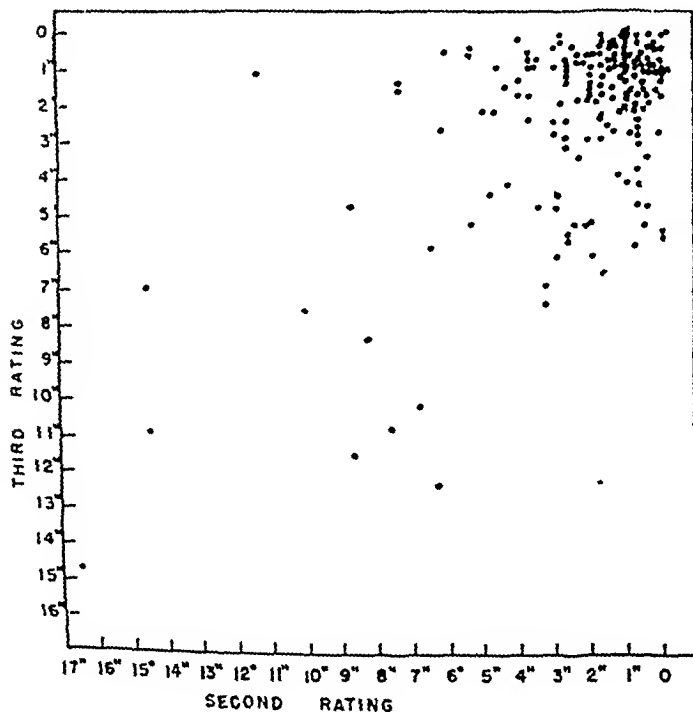


Fig 2—The second and the third Howard-Dolman rating, expressed in terms of absolute deviation in seconds of arc, plotted against each other to indicate their degree of correlation

Only 1 subject (T McG) whose performance was among the 7 poorest on the Verhoeff test was also among the 7 poorest performers on the Howard-Dolman test (table 5). Since the nature of these two tests is such that one measures pure stereopsis while performance on the other depends on many other factors,<sup>4</sup> many subjects may pass the Howard-Dolman test despite a deficiency in acuity of binocular stereopsis. For the same reason, many may fail the Howard-Dolman test and yet be possessed of normal stereoscopic ability, as evidenced by their performance on the Verhoeff test.

Further evidence that a closer correlation exists between pairs of the Verhoeff readings than between pairs of the Howard-Dolman readings is graphically illustrated in figures 1 and 2. In figure 1 the second and the third response in the Verhoeff test, expressed in terms of absolute deviations in seconds of arc, are plotted against each other, and in figure 2 data from the Howard-Dolman test are similarly treated.

#### SUMMARY

A group of 186 subjects whose vision was previously determined to be well within normal limits in several respects was subsequently tested by both the Howard-Dolman and the Verhoeff technic for estimating stereoscopic threshold. The distributions of the averages of three responses to each of these tests are given, and the higher coefficients of self reliability between trials on the Verhoeff test are offered as evidence of the superior efficiency of this test. When the results of each test are translated into terms of absolute deviations in seconds of arc, the responses to the Verhoeff test are found to involve a much wider range than do the results of the Howard-Dolman test, a fact which indicates that the Verhoeff test is the more sensitive in detecting persons with poor stereopsis. The low correlation between the results on these two tests and the number of other factors<sup>4</sup> which enter into the Howard-Dolman performance support the belief that the Verhoeff test yields a superior estimate of acuity of binocular stereopsis. However, the value of the Howard-Dolman technic in the appraisal of aptitude for activities which require a number of attributes, only one among which is stereopsis, in contrast to pure stereoscopic ability, should be kept in mind.

Massachusetts Eye and Ear Infirmary  
Phillips Academy

# THE IRIDENCLEISIS OPERATION FOR GLAUCOMA

ALGERNON B REESE, M D

NEW YORK

The feeling prevails to some extent that it is not a sound surgical procedure to incarcerate iris tissue deliberately for the relief of glaucoma when on all other occasions an effort is made to prevent such an occurrence. I had occasion to review the literature on glaucoma surgery several years ago, and the reports on the iris inclusion operation were so impressive that the procedure was tried. The results have been sufficiently good to warrant continuing the use of the operation more and more during the past three years.

In this period the operation has been performed on my service on 110 eyes, and this report is based on the experience encountered in that series of consecutive operations.

An incarceration or prolapse of the iris under any circumstances may be good or bad, depending on the manner in which it occurs. After operations, especially a cataract extraction, or after perforating injuries, an incarceration may lead to a filtering cicatrix or to secondary glaucoma. If the iris is incarcerated as a wick of tissue with the surfaces of the pigment epithelium together, it is more likely to produce a filtering cicatrix. If the iris is incarcerated in such a manner that aqueous cannot drain out of the wound but dams up in a pocket of iris tissue, which tends to dilate through the effort of the aqueous to escape, then the incarceration does not lead to filtration but predisposes to glaucoma by a tendency of the iris pocket to block more and more of the filtration angle.

When an iridotasis is done, the iris should remain in a position as shown in figure 1*a*. Often, however, the sphincter muscle pulls the pupillary border of the iris partly back into the anterior chamber, as shown in figure 1*b*. This leaves a pocket of iris blocking the wound more and more because of the progressive dilation by the aqueous. This is illustrated in

figure 2, which shows a microscopic section of a human eye on which an iridotasis was performed for chronic glaucoma. Incarceration of the iris in this manner is to be avoided under all conditions—at the time of an iris inclusion operation, as a complication following an intraocular operation or after a perforating injury. After a cataract extraction it is familiar how a knuckle of iris at one site in the wound may at first be so slight that it can hardly be seen but gradually becomes more and more ectatic, with perhaps some gaping of the wound. When an iris inclusion operation is performed, it is important to prevent this type of incarceration of

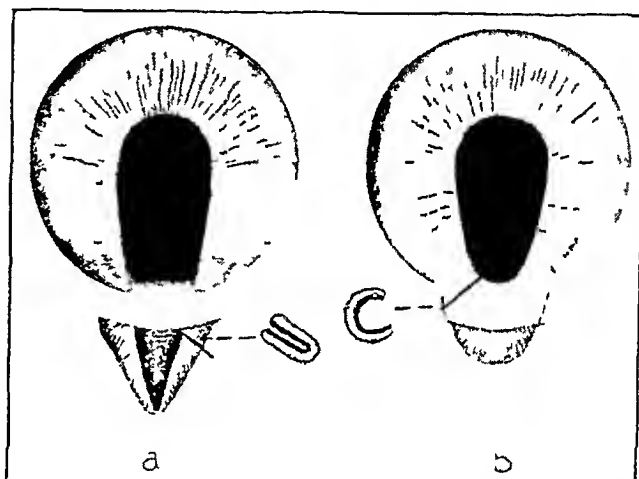


Fig 1—In *a* is shown the position the iris should assume after an iridotasis. The insert is a cross section of one iris pillar to show the manner in which the iris folds.

In *b* is shown the position the iris frequently assumes after an iridotasis. The sphincter muscle has retracted the pupillary margin partly back into the globe, leaving a pocket of iris. The insert is a cross section of the iris over a pillar to show the pocket formed.

This figure as well as figures 4, 5 and 9 are viewed from the surgeon's position at the head of the patient whereas figure 3 is viewed from the spectator's position.

the iris. This can best be done by employing a technic which minimizes such a possibility, and in this regard three features seem important:

- 1 The sphincter muscle must be cut.
- 2 The radial incision in the iris must reach the very periphery of the iris.

From the Institute of Ophthalmology of Presbyterian Hospital.

Read before the New York Academy of Medicine, Section of Ophthalmology, Dec 18, 1944.

3 There should be no root of the iris over the site of the coloboma

The technic here described incorporates these factors

#### TECHNIC

The usual injections for local anesthesia are carried out, including a retrobulbar injection of epinephrine. This is desirable not only to induce anesthesia but to lower the intraocular pressure at the time the anterior chamber is opened. It seems desirable also to wait at least five minutes after the injections are given, as absorption in glaucomatous eyes is slow. It is better to make sure of good anesthesia before the operation is started than to find out that the anesthesia is not adequate when the keratome is in the anterior chamber. A keratome section is made under a large conjunctival flap. The point of the keratome engages the con-

into the corner of the wound with a minimum amount of manipulation. The conjunctiva is closed with interrupted silk sutures. Drops are not instilled.

#### DISCUSSION OF THE OPERATION

The most important step in the operation is a correct incision. This should be made far back so that the point of the keratome enters the anterior chamber in or close to the angle (fig 5a and a'). This is the type of section advocated by R G Reese<sup>1</sup> for iridectomy in cases of glaucoma. If the section is placed properly in

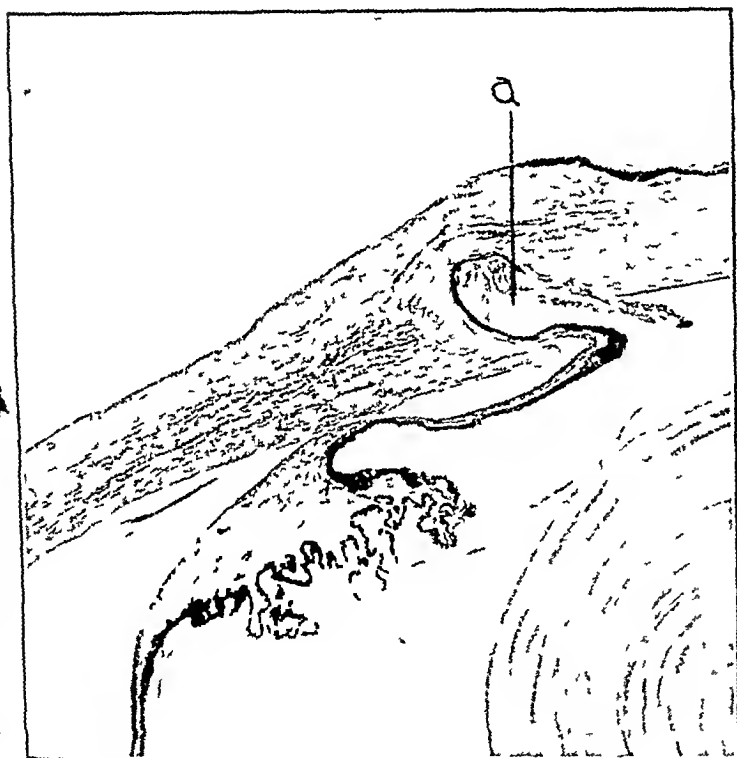


Fig 2—An iridotaxis for chronic glaucoma. The incision is placed too far centrally. The pupillary margin of the iris has retracted into the globe, leaving the pocket of iris (a) dilated with aqueous.

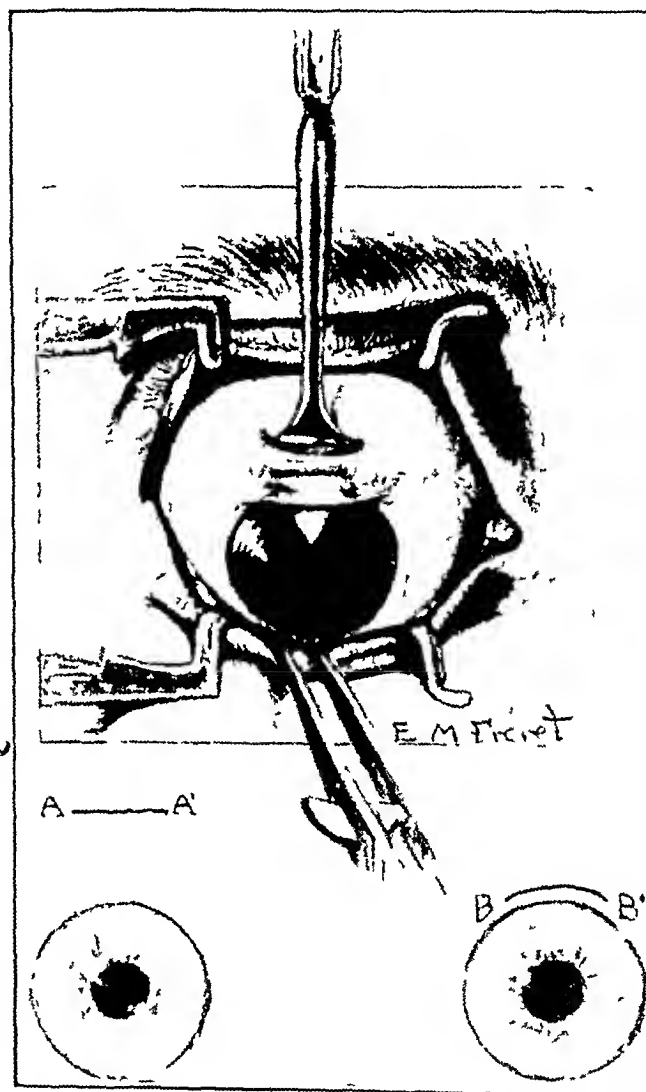


Fig 3—The incision, with the keratome under a conjunctival flap. A-A' indicates the position of the incision through the conjunctiva, B-B', the position of the incision through the sclera.

This figure is viewed from the spectator's position whereas figures 1, 4, 5 and 9 are viewed from the surgeon's position.

the periphery of the anterior chamber, the point of the keratome will sometimes engage the iris and push the iris ahead of it, thus producing an iridodialysis. This is desirable rather than otherwise, for it shows that the section is well placed and the iridodialysis does not have to be

1 Reese, R G. A Conjunctival Flap for Glaucoma, Using a Broad Keratome, *Tr Sect Ophth*, A M A, 1923, p 317.

conjunctiva at least 10 mm from the limbus, and the conjunctiva is dragged down over the point of the keratome to within 2 mm or more of the limbus, where the point then engages the sclera. The incision is completed by entering the keratome at least three-fourths the length of its blade into the anterior chamber (fig 3). The conjunctival opening is enlarged on each side with scissors. The operator withdraws the iris by grasping it at the pupillary margin. An assistant holds the iris on the opposite side, and in unison they withdraw the iris until an iridodialysis is just noted (fig 4a). Then a radial cut is made through the iris into the iridodialysis opening (fig 4b). The assistant releases the iris, and the operator then incarcerates each pillar

performed later. A shelving of the cornea with the entrance of the point of the keratome in corneal tissue predisposes to failure of the operation (fig 5*b*). Figures 2, 6 and 7 show faulty incisions in human eyes with primary glaucoma.

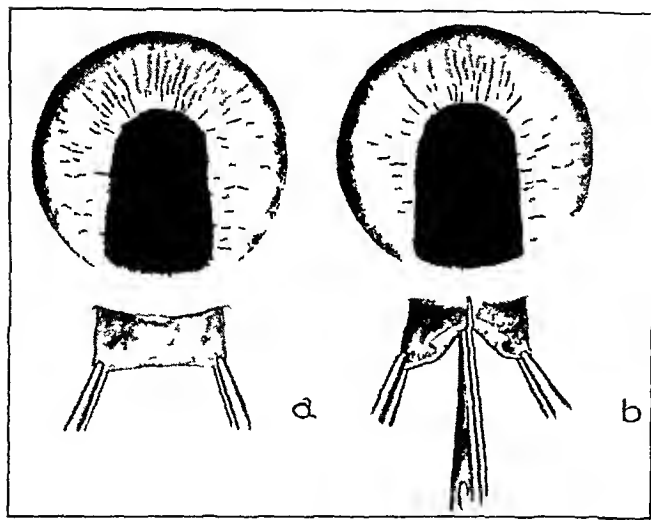


Fig 4—In *a*, the iris is being withdrawn until an iridodiolysis is produced. The iridodiolysis is shown at the center, adjacent to the wound. In *b*, the radial cut is being made into the iridodiolysis opening, the stroma of the iris curls around the pigment epithelium.

Microscopic preparations show that most keratome sections for glaucoma are placed too far on the corneal side and that advantage is not taken of the wide margin of safety by making them more peripheral.

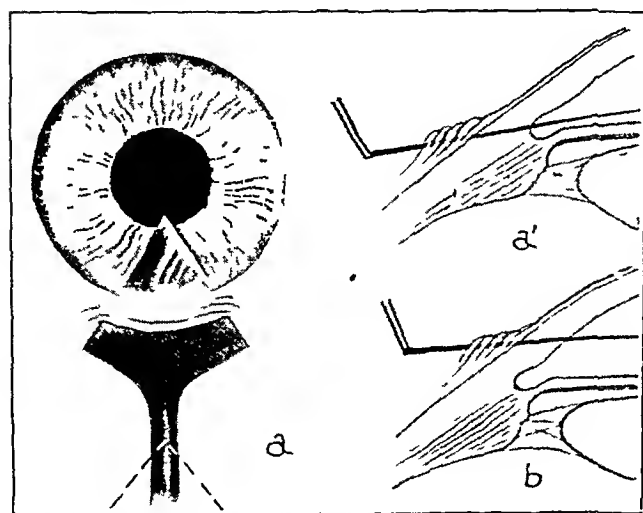


Fig 5—In *a*, a keratome section is made under a conjunctival flap 2 mm or more back of the limbus. The dotted lines show the point at which the keratome engages the conjunctiva. A cross section (*a'*) shows the keratome at the proper position in the anterior chamber.

In *b*, the keratome is in the anterior chamber too far on the corneal side.

It is frequently said that the iridencleisis operation is easy, and sometimes that is a disadvantage rather than an advantage. If it were so, it would be a distinct advantage, but it is not altogether true. I should say that the operation is a short and simple procedure but not an easy one. The important step of the operation is the incision, and it is not easy to make this correctly. I have seen more ophthalmic wrecks from poorly executed keratome sections for glaucoma than I have from improperly executed tiaphine operations.

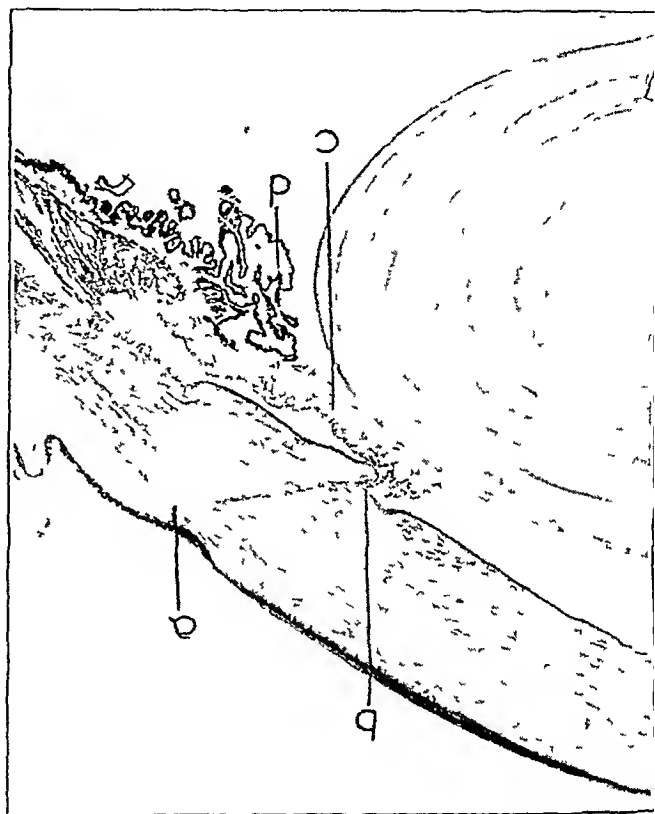


Fig 6—Keratome section for glaucoma extending from *a* to *b*. The section is so far on the corneal side that there is hardly sufficient iris *c*, to reach subconjunctivally. Edematous ciliary processes are shown at *d*.

It cannot be argued that peripheral synechias prevent the execution of the section as advocated, because if the operation is carried out only in those cases in which it is indicated, as specified later, peripheral synechias will not be encountered, as they are to be expected in the later stages of glaucoma.

The conjunctival flap made with the keratome is better than the dissection of a flap because such a flap has a minimum amount of scar tissue and this is desirable for a flat, diffuse, filtering bed. The radial cut in the iris must reach the periphery of the iris to prevent the

root of the iris from blocking the angle or forming a pocket over the operative site. These aims can best be accomplished by producing an iridodialysis and having the radial cut extend into it. When the iridodialysis is produced, the iris always tears flush with the ciliary body, leaving no root, because it is here that the iris is thinnest, and also weakest, from the presence of the peripheral crypts. Figure 7 shows the manner in which the iris severs from the ciliary body when torn. It is undesirable to try to arrange the iris pillars too much, for trauma tends to

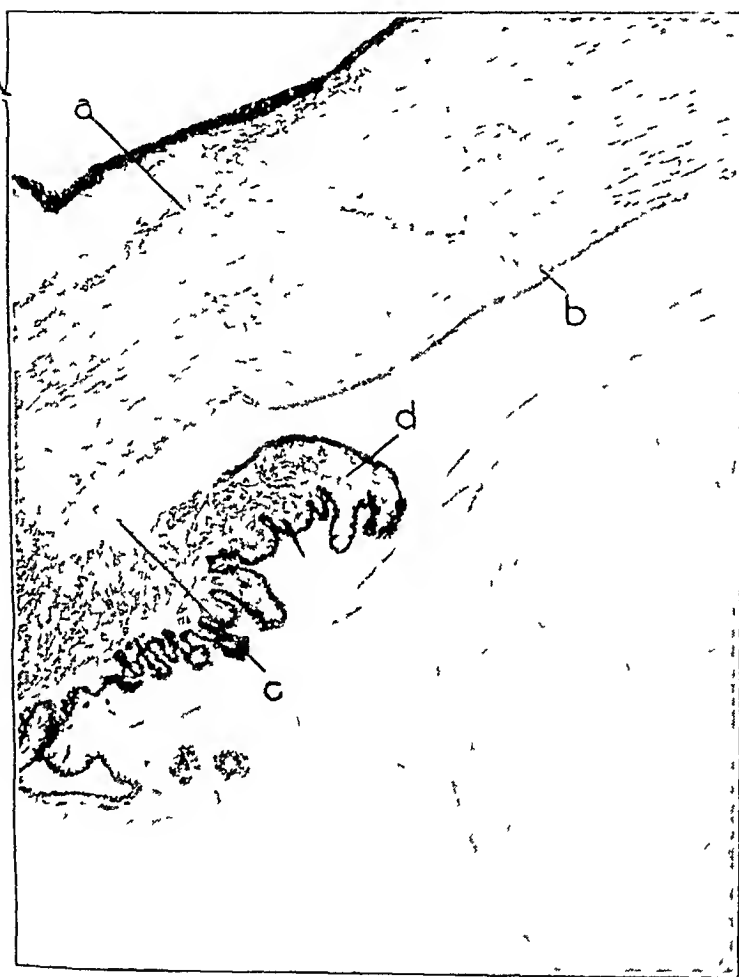


Fig 7—Keratome section for glaucoma extending from *a* to *b*. The section is placed too far toward the cornea. The iris was torn from its insertion into the ciliary body, at *c*. Edematous ciliary processes are shown at *d*.

stimulate the iris tissue to repair by the production of fibrous tissue. Furthermore, every precaution should be taken not to abrade the pigment epithelium. The wick of iris produced by that portion of the iris over the site of the iridodialysis seems to fall in the desired manner naturally. This is with the pigment epithelium inverted, with the curled stroma forming the outer surface (figs 4*b* and 9 *B-B* insert). The fact that free, normal iris tissue tends to assume this position is evidenced by sections of iris

tissue removed for whatever cause. In a recent case in which there was a small malignant melanoma of the iris a broad iridectomy was done. The iris was allowed to curl according to its inclination, and a section of this is shown in figure 8.

It is perhaps worth while to separate the lips of the wound by grasping the conjunctival flap at the time when the wicks of iris are placed in the angles of the incision, so that the iris tissue will be free to curl in the desired manner at the site where they pass through the wound. It is desirable to incarcerate both pillars. This seems to insure more adequate drainage and does not give hypotony.

When the operation is carried out as outlined, a section through the coloboma (fig 9 *A-A*) should show the relations as depicted in figure 9*a*, i. e., the incision in the periphery and no iris root. A section through the iris pillar (fig 9 *B-B*) should show the relation as depicted in figure 9*b*, i. e., the incision in the periphery and the wick of iris extending straight out the incision to the subconjunctiva. A cross section of the wick of iris in an inset opposite one of the pillars shows the pigment epithelium lining the curled stroma.

#### FUNCTION OF THE OPERATION

The operation is effective primarily because the wicks of iris produce a vicarious filtering sluiceway. A lesser factor contributing to the effectiveness of the operation is the iridodialysis, which frees the angle over the coloboma area. This gives the effect of a basal iridectomy. Another factor seems to be the occurrence of a taut iris below, that is, when the iris is pulled up and out of the wound above, the iris below is put on some stretch, which widens the angle. The tautness of the iris also, no doubt, tends to prevent the iris from blocking the filtration angle. This widening of the angle below, due to the tautness of the iris, is borne out by gonioscopic examination.

#### INDICATIONS FOR THE OPERATION

The iridencleisis operation cannot be relied on to carry too much of a drainage load. It seems to be indicated therefore in cases of glaucoma with a peak pressure of 40 to 45 or maybe 50, mm of mercury on the Schiötz tonometer and a basal pressure of 30 mm of mercury or less. It is frequently not adequate in cases of glau-



coma with much higher pressure. In such instances, however, an iridencleisis operation can be combined with a sclerectomy. This was done in 3 instances and proved effective. The operation is indicated in every case of primary glaucoma in the Negro, and aside from iridectomy for true acute glaucoma, it is the only operation that is effective in persons of this race. It may be used for secondary glaucoma in eyes with inactive uveitis. It has been surprising how well the operation is tolerated in eyes in which the uvea was the seat of an inflammation. In 2 instances the inflammation seemed not entirely inactive, but still the operation was effective and well tolerated. It seems as effective as any other operation in cases of hydrophthalmos and buphthalmos.

iridectomy is adequate. In cases of acute exacerbation of chronic glaucoma, the operation could be used if none of the contraindications is present. It is not indicated in cases of glaucoma in aphakic eyes.

#### RESULTS

Statistics on glaucoma are difficult to evaluate and compare because so much depends on the stage of the disease at which the operation is done, on the duration of the follow-up period, on the type of glaucoma and on whether or not the operation is primary or secondary to other operations.

As the indications for the operation became more apparent, it has been restricted more and more to cases of the type indicated in this paper.

The statistics presented here are based on

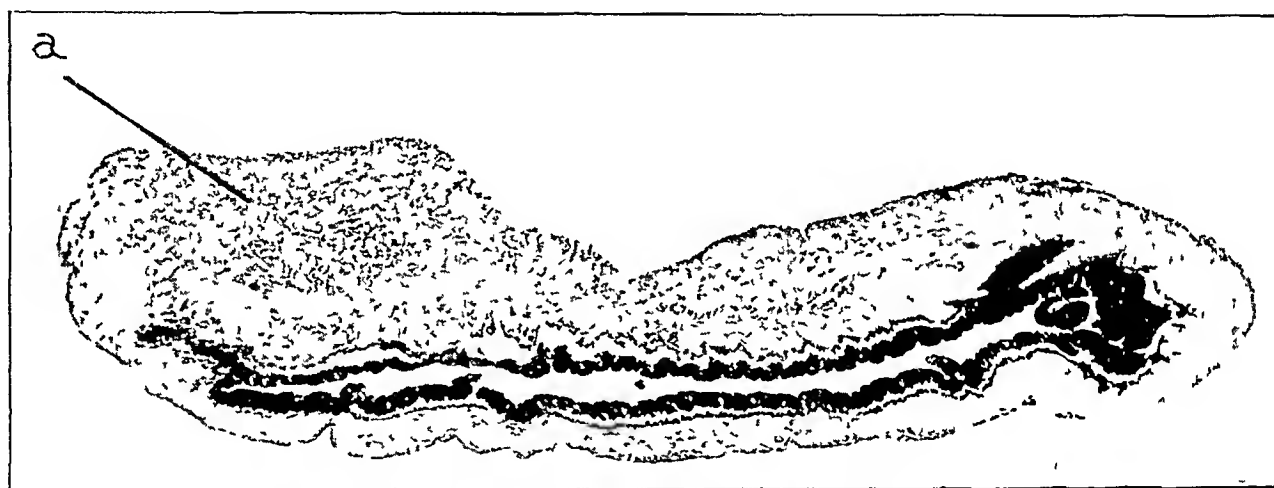


Fig 8—Normal iris curling to form a wick, the central lumen of which is lined with pigment epithelium (The specimen is a portion of iris removed because of a malignant melanoma. The periphery of the tumor is shown at *a*.)

#### CONTRAINDICATIONS TO THE OPERATION

In cases in which one or more operative procedures have failed, the use of the iridencleisis operation has not proved satisfactory. This may be due to the fact that in most instances the drainage load necessary for the operation to carry is too great. It also is not satisfactory in cases of long-standing glaucoma in which not only is the pressure high but secondary changes in the iris, such as vascularization and atrophy, have occurred. In glaucomatous eyes the iris stroma is replaced by connective tissue as the disease advances, and such irises when incarcerated probably produce fibrous tissue, which tends to close the filtering area. A relatively normal iris has little or no tendency to the formation of repair tissue. I have never used the operation in cases of acute glaucoma because for them

61 operations which I performed on private patients, as the records of these patients lend themselves better to analysis.

The disease was considered arrested if the postoperative intraocular pressure was never higher than 27 mm of mercury with the Schiötz tonometer one month after the operation. The results were reckoned after the lapse of this postoperative period because in a few instances it was noted that the intraocular pressure fluctuated somewhat above normal for a few weeks after operation and then leveled off to normal and remained there. In 1 instance the postoperative pressure was found to be above normal several times for a postoperative period of two months and then became normal.

With these criteria, the disease was deemed arrested in 52 of the 61 eyes, or in 85 per cent.

It is true that some of the patients have not been followed for a sufficiently long postoperative period.

An analysis of the 9 cases of failure shows that in 7 of them the operation was contraindicated according to the stipulations in this paper. These 9 cases may be summarized as follows:

Case 1—Secondary glaucoma with retinal detachment from retinitis proliferans. The intraocular pressure was 70 mm of mercury. The eye was blind and painful. Permission for enucleation was refused.

Case 2—Secondary glaucoma from an iridocyclitis which was somewhat active.

Case 3—Primary glaucoma, for which four trephine operations had been done before the iris inclusion operation.

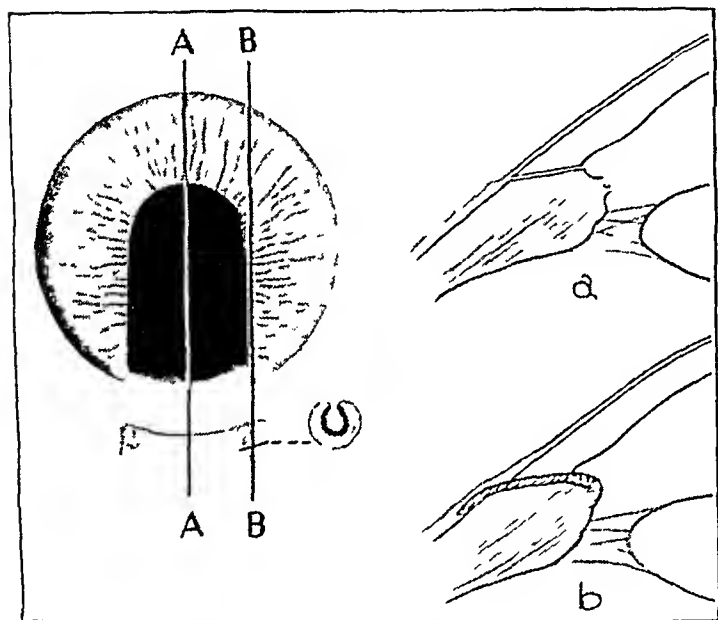


Fig 9—A section through the coloboma at A-A would appear as shown in a. A section through the pillar at B-B would appear as shown in b. The insert shows a cross section of the wick of iris.

Case 4—Primary glaucoma in a Negro. One trephine operation had been done before the iris inclusion operation.

Case 5—Same patient as that in case 4. A second iridencleisis was done.

Case 6—Primary glaucoma, for which a trephine operation failed before the iris inclusion operation was done.

Case 7—Primary glaucoma with an intraocular pressure of 70 mm of mercury. The iris was semidilated and immobile from atrophy.

Case 8—Primary glaucoma with no contraindication to the operation. The failure of the operation was attributed to a poorly placed incision.

Case 9—Primary glaucoma with no contraindication to the operation. The failure of the operation was attributed to a poorly placed incision.

If the intraocular pressure was as high as 27 mm of mercury at any time during the follow-up period, a miotic was prescribed as a precautionary measure, to be used twice daily. This was necessary in 29 per cent of the cases of arrested glaucoma. Of the cases in which the operation was successful, the difference between the mean of all of the preoperative pressures and the mean of all of the postoperative pressures was 18.7 mm of mercury, i. e., the operation effected a mean reduction of 18.7 mm of mercury in the intraocular pressure. It has been stated that the operation is indicated in cases with a peak pressure of 45 and perhaps 50 mm of mercury. Subtracting the mean reduction of 18.7 mm from 50 mm leaves 31.3 mm. Selecting 45 to 50 mm of mercury as the peak pressure is, therefore, on the conservative side, because the peak pressure is appreciably higher than the mean pressure.

#### ADVANTAGES OF THE OPERATION

I believe that the best way to arrest glaucoma is to operate at the earliest possible time<sup>2</sup> after it is clear that an operation is indicated. This usually means that the operation is done when the patient still has normal vision and normal, or almost normal, fields. The large majority of patients with glaucoma are practically symptomless. Therefore it is usually necessary to advise an operation on a patient with normal vision, normal fields and no symptoms. The patient is offered no tangible result, as is the patient with cataract or squint. He is offered only the hope that the vision can be saved for the future. When I advise an operation in such a situation, I like to feel not only that there is an excellent chance of arresting the disease but that there is a negligible chance of any complications being created. This is definitely my feeling in regard to the iridencleisis operation, but not so in regard to the trephine operation, which is too frequently followed by quiet iritis, slow restoration of the anterior chamber, detachment of the choroid, hypotony, a redundant filtration bleb, progressive changes in the lens or late infection.

There are really no serious complications following an iridencleisis operation. Sometimes mild iritis manifests itself as a slight proliferation of pigment around the pupillary margin and a

2 Reese, A. B. The Value of Early Operation in Chronic Primary Glaucoma, J. A. M. A. **113** 1204 (Sept. 23) 1939.

slight tendency to posterior synechias. This feature, however, has never proved serious. Sometimes there is a hyphemia, but this absorbs and has never caused any untoward consequences. The hyphemia may be the cause of a somewhat elevated intraocular pressure for a time after the operation.

Eyes with primary glaucoma are more predisposed to the development of cataract than nonglaucomatous eyes. One third or more of the eyes with primary glaucoma have incipient cataractous changes. Operations for glaucoma in general, and especially the trephine operation, tend to hasten the development of these incipient cataractous changes. An analysis of the cases in which the iridencleisis operation has been done seems to indicate that this procedure predisposes less to the progression of incipient cataractous changes than any other operation for glaucoma except the straight iridectomy. In no case has hypotony, detachment of the choroid, slow restoration of the anterior chamber, a redundant filtration bleb or late infection been noted.

#### DISADVANTAGES OF THE OPERATION

The possibility of sympathetic inflammation is frequently mentioned in connection with this operation. This complication has not appeared in the present series of cases, nor has it occurred in a series of over 200 cases at the Illinois Eye and Ear Infirmary.<sup>3</sup> Every intraocular operation has a very high incidence of incarcerated uveal tissue of some degree and a very low incidence of sympathetic inflammation. From my experience alone I have no reason to feel that the incidence is any higher in the one intraocular operation than in the others. I am inclined to believe, however, that in the long run the incidence of sympathetic inflammation must be somewhat higher after the iris inclusion operation than after other intraocular operations but that it is not sufficient to be a serious contra-indication to the operation.

Sometimes the question of a pulled-up, or hammock, pupil is mentioned. There is a tendency for the pupil to be higher, but at no time has this feature been sufficiently pronounced to be of consequence.

<sup>3</sup> Kronfeld, P. Personal communication to the author.

A cataract extraction is perhaps made somewhat more difficult by this type of operation.

Also, if a trephine operation is done on an eye which has been subjected to an iris inclusion operation, the iris tends not to prolapse after the trephining if the site of the operation is over one of the iris pillars. This is due to the fact that the tautness of the pillar prevents the iris from prolapsing to any extent, if at all.

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#### DISCUSSION

DR ARNOLD KNAPP, New York. Several things in Dr. Reese's demonstration interested me particularly. I had long had the idea that one of the advantages of the iridencleisis operation was that it was an easy procedure, as the section was made at the limbus, but Dr. Reese stresses the making of the incision 2 mm back of the limbus, a method which in the chronic glaucomatous eye is often very difficult. Furthermore, Dr. Reese produces an iridodialysis and believes that he is tearing the iris at its root. With chronic glaucoma, however, the angle of the anterior chamber is obliterated, and one cannot get at the root of the iris. Dr. Reese has not made clear why he has abandoned the operations for chronic glaucoma which have given such good results—the Lagrange and the modified trephine operation. I have always felt that iridencleisis should be done as a last resort, and then combined with sclerectomy.

DR KAUFMAN SCHLIVEK, New York. When the iridencleisis operation was introduced in Vienna, several years ago, I saw many cases and was much discouraged with the results. A few years ago I saw the operation performed in another hospital in a case in which sympathetic ophthalmia developed. My experience with this operation has been slight. In the few cases in which my associates and I have performed it the results have not been satisfactory, but in our institution we always follow the rule: acute glaucoma, iridectomy; secondary glaucoma, Lagrange operation; chronic simple glaucoma, trephination or, if the iris is atrophic, trephination with complete iridectomy.

DR DAVID H. WEBSTER, New York. I have limited this operation to cases of infantile glaucoma. It has been the only procedure in which I have succeeded in controlling the tension and retaining vision. In cases of infantile glaucoma the iris is elastic except those in which the disease is accompanied with other degenerative changes and no operation seems to succeed, but in the average case of infantile glaucoma, in which the cornea

measures from 15 to 16 mm, even though the cornea is milky white, the iris can easily be grasped, pulled into the wound, separated at the root and incised and the divided pillars left under the conjunctiva

DR ROBERT K. LAMBERT, New York During the past year my colleagues and I have employed iridencleisis much more frequently than was formerly done on the eye service at Mount Sinai Hospital, and we have usually had good results

DR JOHN MCLEAN, New York I have been seeing and doing this operation a little longer than Dr Reese, for about ten years, during which time I have seen, though they were not mine, 3 cases of sympathetic ophthalmia following iridencleisis I have also seen cases of sympathetic ophthalmia following iridectomy, trephining and cataract extraction The incidence following iridencleisis has been sufficiently low not to influence me to discontinue the use of this operation, but I am sure that if Dr Reese continues to do this operation he will encounter the complication sooner or later

As to the ease or difficulty of the operation, with the keratome incision (which is only one of several ways in which it may be done) there will not be much difficulty if the cases are limited to those indicated by Dr Reese as suitable, among others, those of early glaucoma in which the tension has not become too high, for in most such cases there will not be very shallow chambers or extensive anterior peripheral synechias and there will be room to make a fairly easy keratome incision, about 1.5 to 2 mm back of the limbus

I should like to make one other suggestion, namely, that another good reason for doing this operation in suitable cases is that for the occasional operator it is really much easier than trephining, or even the various modifications of the Lagrange operation

DR HENRY MINSKY, New York I should like the privilege of making a few remarks, especially since Dr Reese pointed out many years ago, as he did tonight, that the selection of the site of the keratome incision is one of the important steps in the operation Also, Dr Knapp has raised the question of the difficulty of the keratome incision, as has Dr McLean, in cases of the late stages of glaucoma For years I have taught a simple method of selecting the site of the keratome incision which makes the operation easy for the novice, as well as for an experienced operator If the contralateral point on the limbus is illuminated by focal illumination, as is done in examination with the slit lamp, a brilliant crescent appears at about 12 o'clock at the extreme

periphery If the point of the keratome is entered in the sclera at the very edge of the illuminated crescent and the keratome sent home in the plane of the iris, the surgeon will inevitably hit the angle of the anterior chamber just anterior to the ciliary processes and perform the peripheral incision at the limbus, so as to get the root of the iris without fail If that is done, the necessity of tearing the root of the iris may perhaps be avoided, for when the incision is made in the manner suggested the iris is easily grasped, pulled into the wound and put into position

The mere specification of 1.5 or 2 mm from the limbus is not sufficient, because the measure is an arbitrary one and the position of the limbus varies in each eye, especially in the glaucomatous eye One can easily find the precise angle of the anterior chamber and make the iridencleisis more successful by the method of the incision suggested

DR ALGERNON B. REESE, New York Dr Knapp said that one of the virtues of the operation was that it is easy to perform The procedure is a simple one, but I do not believe it is particularly easy to make a correct incision far in the periphery of the anterior chamber — and this is the most important feature of the operation

Dr Knapp also stated that in the eye with chronic glaucoma the angle is obliterated and therefore one cannot produce an iridodialysis as described If there are peripheral synechias, the operation is not indicated, for synechias do not occur except in advanced glaucoma I think synechias are likely to be the exception in the eyes which are operated on for glaucoma in general, and if they are present the glaucoma is in an advanced stage In cases of this type some other operation which will carry a greater drainage load is indicated

I have not given up the trephine, cyclodialysis and Lagrange operations but use them only in indicated cases

Dr Schlivek brings up the question of sympathetic inflammation This presentation is based on my personal experience with the operation In this series of 110 operations we have had no case of sympathetic inflammation The incidence of this complication may be higher in this operation than it is in other intraocular procedures, but my experience does not bear this out

Dr Schlivek states that he has not done this operation on many eyes I think this is in accord with the experience of most of us in this section We have been loath to adopt this operation, and in some measure it is heresy to expound the virtues of the operation

Dr Webster mentioned that the operation is useful in cases of hydiophthalmos. Dr Sanford Gifford also expressed this view in an article several years ago. I have performed the operation in 2 such cases, in both it worked well. There were, however, rather large redundant blebs in both instances.

Dr McLean also brings up the question of sympathetic inflammation. I agree with him that sooner or later I shall encounter sympathetic ophthalmia as a consequence of the operation. In the meantime, however, I hope to have arrested more cases of glaucoma.

Dr McLean also states that the operation is an easy one. If so, this is a virtue and not a fault. I contend it is a simple procedure but not an easy one to execute correctly. I believe more eyes are ruined by a poorly executed keratome section for glaucoma than by the trephine operation.

Dr Lambert mentions some good results he has had with the operation.

Dr Minsky brings out a good point regarding the placing of the incision.

# EFFECT OF TALC IN OCULAR SURGERY

MAX CHAMLIN, M D

NEW YORK

Since rubber gloves have become popular in the operating rooms of many ophthalmic institutions, one is prompted to study the effect on the ocular tissues of the talc powder on these gloves. There has been a great deal of investigation along these lines, starting in 1933, when Antopol<sup>1</sup> reported the formation of tubercles by spores of *Lycopodium*. At that time the spores of *Lycopodium* were used on surgical gloves, as talc is used today. However, even as far back as 1912, Lambert<sup>2</sup> reported a foreign body giant cell reaction to spores of *Lycopodium*. He used the substance as a nonspecific foreign body and stated that he could just as well have used cotton fibers, or even glass.

In later years, when talc had largely replaced spores of *Lycopodium*, similar investigations were conducted by various workers with the express purpose of determining the effect that accidental introduction of talc from surgical gloves produces on tissues. The main constituent of talc is magnesium trisilicate, which composes about 60 per cent of the substance. Correspondence with various manufacturers revealed fairly uniform qualitative and quantitative analyses of the talc powders. The talc used in the present study was obtained from Chas. B. Crystal Co., Inc., who furnished the following quantitative analysis:

	Per Cent
Silica (magnesium trisilicate)	60.04
Aluminum oxide	1.80
Iron oxide	0.16
Calcium oxide	0.38
Magnesium oxide	30.98
Loss on ignition	6.22

In general, the various investigators in the field have reported fairly uniform results. The crystals of magnesium trisilicate were found in large granulomatous masses which were produced by the experimental introduction of talc

in animal and human tissues. Such observations have been reported by Ramsey and Douglass,<sup>3</sup> de Savitsch,<sup>4</sup> Byron and Welch,<sup>5</sup> German<sup>6</sup> and several others.

The granulomas produced by talc were found to cause the clinical picture of tumor, the mass being even large enough to produce intestinal obstruction in some cases. In other cases visceral adhesions were formed. In view of such observations, it seemed important to determine whether similar reactions occur in the eye, as no such studies have been reported. Tumors of any size produce more serious sequelae in a compact, enclosed organ such as the human eye, in which all physiologic functions are dependent on fine anatomic structures.

One series of studies consisted of the withdrawal of varying amounts of aqueous from rabbit eyes and the replacement with similar amounts of suspension of talc of varying concentration in isotonic solution of sodium chloride. The second series consisted of iridectomies with irrigation of the anterior chamber with suspension of talc in saline solution, in two concentrations. In the third series, varying amounts of a suspension of talc were injected between the extraocular muscles and the sclera. By using these three methods of introduction of talc my associates and I planned to simulate the accidental introduction of talc into ocular tissues during surgical procedures.

## TECHNIC

In order to avoid extraneous factors, the procedures were made as simple as possible and were carried out with local anesthesia and with aseptic precautions. The rabbit was placed in a small wooden operating box, and the assistant immobilized the head with one hand.

3 Ramsey, T. L., and Douglass, F. M. Granulomatous Inflammation Produced by Foreign Body Irritants, *J. Internat. Coll. Surgeons* **3**: 3-10 (Feb.) 1940.

4 de Savitsch, E. Granuloma from Penetration of Talcum Powder, *M. Ann. District of Columbia* **9**: 169-170 (May) 1940.

5 Byron, F. X., and Welch, C. S. Complications from Use of Glove Powder, *Surgery* **10**: 766-769 (Nov.) 1941.

6 German, W. M. Dusting Powder Granulomas Following Surgery, *Surg., Gynec. & Obst.* **76**: 501-507 (April) 1943.

From the Ophthalmological Service of Montefiore Hospital for Chronic Diseases.

1 Antopol, W. *Lycopodium* Granuloma, *Arch. Path.* **16**: 326-331 (Sept.) 1933.

2 Lambert, R. A. The Production of Foreign Body Giant Cells in Vitro, *J. Exper. Med.* **15**: 510-515, 1912.



and with the other inserted a thin metal tongue depressor outside the lower lid, between the globe and the orbital floor. With exertion of firm, but gentle, pressure toward the apex of the orbit, the globe was proptosed. Several instillations of 0.5 per cent tetracaine hydrochloride were made before and after proptosing the eye. If the tongue depressor was kept in place, the globe not only remained proptosed but was immobilized. This approach made the eyes accessible to our procedures. No general anesthetic was used. In performing the iridectomies with local anesthesia, we were concerned about the pressure exerted in proptosing the globe with the assistant's tongue depressor. However, once the globe was proptosed and the pressure with the tongue depressor somewhat relaxed, the globe rotated into its "anatomic" position and remained proptosed, while the tongue depressor was kept loosely inserted between the globe and the lower orbital wall, with practically no pressure exerted on the eyeball.

#### PROCEDURES AND RESULTS

**First Series Introduction of Talc into Anterior Chamber**—Three rabbits were used in this series of studies. Varying amounts of aqueous were withdrawn from the anterior chamber into a syringe and replaced with similar amounts of suspensions of talc, of varying concentrations, in isotonic solution of sodium chloride. In the control eye, saline solution was used instead of the suspension of talc. As the table indicates, all the eyes in which suspension of talc was injected showed reactions, of varying degrees. At first, the talc settled to the lower angle of the anterior chambers in a crescent-shaped distribution. This mass was eventually replaced with a granuloma in 3 eyes. Two eyes showed only a number of foreign body giant cells under the endothelium of the iris. That portion of the cornea which was in contact with the talc exhibited some vascularization. The control eye, 5R, did not show any of these inflammatory reactions.

**Second Series Iridectomy with Irrigation of Anterior Chamber with Suspension of Talc**—In this series, 4 rabbits were used, the iridectomy being performed on one eye of each animal. In 3 of the eyes the anterior chamber was irrigated with a suspension of talc, and in the control eye saline solution was used. It is interesting to note that yellowish exudate was formed at the site of the coloboma. That is, the foreign body reaction was more pronounced in those tissues which had undergone surgical trauma than in the lower angle of the anterior chamber, to which the talc gravitated in the first series and in which no intraocular operation was performed. This observation coincides with the experience of German.<sup>6</sup> This author found that foreign body granulomas due to talc were more apt to form on tissues that had undergone sur-

gical trauma than on smooth serous surfaces. In the control rabbit there were no exudates of any kind. In all these rabbits the use of atropine or any other drug was avoided so as not to influence the postoperative course more than was necessary.

**Third Series Submuscular Injection of Talc**—In this series, 3 eyes were used. Actual operation on the muscle was avoided so that the reaction should depend as much as possible on the talc alone. Varying amounts of suspension of talc were injected under the superior rectus muscle in each eye. This was done through a small nick in the conjunctiva and Tenon's capsule, at a little distance from the muscle. A needle of the type used to irrigate the lacrimal sac was introduced along the smooth scleral surface to a position beneath the belly of the muscle, which was easily visualized through the thin conjunctiva. In all cases granulomatous masses were produced beneath the muscles.

#### ENUCLEATIONS

Enucleations were carried out with intravenous injection of veterinary pentobarbital sodium one month after the initial procedures. Most of the animals required 5 cc of veterinary

*Data on Experimental Introduction of Talc in Rabbit Eyes*

Rabbit and Eye No	Procedure		Clinical Reaction in 14 Days *	Histologic Reaction †
	Aqueous Withdrawn, Cc	Amount of Talc Sus- pension Injected Into Anterior Chamber		
Series 1 Talc in Anterior Chamber				
4R	0.05	0.05 cc of 0.03%	+++	++
4L	0.10	0.10 cc of 3.0%	+++	++
5L	0.10	0.10 cc of 0.5%	+	++
7R	0.20	0.10 cc of 3.0%	+++	+++
7L	0.10	0.10 cc of 0.5%	+	+
5R	0.10 (con- trol)	0.10 cc of 0.5%	—	—
Series 2 Iridectomy and Irrigation with Talc				
1R	Irrigation of anterior chamber with 0.5% talc suspension		+++	+++
3R	Irrigation of anterior chamber with 1.0% talc suspension		++	++
9R	Irrigation of anterior chamber with isotonic solution of sodium chloride (control)		—	—
Series 3 Talc Injected Submuscularly				
10R	0.3 cc	} of 10 % talc suspension injected between muscle and sclera	+++	++++
11R	0.2 cc		++	+++
11L	0.3 cc		+++	+++

\* In this column, — indicates no inflammatory reaction, +, a slight inflammatory reaction (uveal or submuscular), ++, moderate inflammatory reaction (uveal or submuscular), +++ moderate inflammatory reaction, with mass in the anterior chamber or under the muscle, and ++++, marked inflammatory reaction, with large mass in anterior chamber or under the muscle.

† Here, — indicates no reaction, + foreign body giant cells under endothelium of the iris, ++, foreign body giant cells and fibrosis, +++ moderate foreign body granuloma formation and ++++ large foreign body granuloma formation.

pentobarbital sodium (0.065 Gm per cubic centimeter) for the enucleation. The eyes were fixed in Bouin's solution and, after the usual dehydration with alcohol and xylene, were embedded in paraffin and stained with hematoxylin and eosin.

## COMMENT

In studying the table, one can readily see that talc did produce foreign body granulomas in the majority of the eyes. Three of the 5 eyes (7 R, 4 R, 4 L) which had talc inserted into the anterior



Fig 1 (eye 7R)—Foreign body granuloma in the angle of the anterior chamber produced by injection of talc into the chamber. A indicates the cornea, B, a foreign body granuloma in the angle of the anterior chamber, with fibrotic adhesions to Descemet's membrane, anteriorly, and to the iris, posteriorly, C, the iris, and D, the cilio-scleral sinus, first described by Troncoso (ARCH OPHTH 31 481-502 [June] 1944)



Fig 2 (eye 10R)—Foreign body granuloma on the outer surface of the sclera. A indicates a granulomatous mass under the subconjunctival tissue, B, episcleral tissue, C, the sclera, and D, the ciliary body.

chamber showed formation of granulomatous masses (fig 1). In the other 2 eyes some foreign body giant cells were noted under the endothelium of the iris, together with swelling of the ciliary epithelium. In the second series, the 2 eyes which were irrigated with a suspension of talc after iridectomy showed a foreign body giant cell reaction, with a granulomatous mass in 1 of them (1 R). The control eye (9 R) did not show any foreign body giant cells. In the third series, all 3 eyes which had talc inserted under the muscle showed a foreign body granuloma at the site of injection (fig 2).

Our observations show that the extent of the reaction, as observed clinically and histologically, does not necessarily correspond to the quantity of talc introduced into the eye. For instance, as seen in the table, eye 4 R in which less talc was inserted showed a far greater reaction than did eye 5 L, which received a greater amount of talc. Furthermore, when the aqueous was completely removed prior to the introduction of talc, the reaction was most severe. I ascribe

this to the greater protein content of the secondary aqueous. As a matter of fact, in preliminary studies, in which varying amounts of aqueous were withdrawn from rabbit eyes, in general the more aqueous was withdrawn the greater tendency there was to formation of fibrin coagulum. Therefore, when the anterior chamber was completely empty, the protein content of the secondary aqueous was greatest and a more severe reaction followed.

Microscopic study of the granulomatous masses revealed a similar cytologic picture in most of the eyes. Essentially, the reaction was that of an inflammatory mass consisting of polymorphonuclear leukocytes, talc crystals (fig 4), foreign body giant cells, some small round cells and fibrous tissue. The foreign body giant cells (fig 3) contained large talc crystals or debris from talc in various states of disintegration. Varying amounts of fibrin were found along the outer layers of the granulomas, binding the mass to the adjacent tissues. Thus, in



Fig 3 (eye 10R)—Multinucleated foreign body giant cells from a granuloma under muscle. A indicates multinucleated giant cells, with disintegrating talc within.  $\times 200$

the angle of the anterior chamber, one found fibrin binding the mass to corneal endothelium, on one side, and to the anterior surface of the iris, on the other, with destruction of iris tissue by scar formation (fig 1). The swelling of the ciliary epithelium was fairly uniform in all the eyes in which talc was introduced intraocularly. In the eyes with least reaction, eye 5 L for example, only some foreign body giant cells were found beneath the anterior endothelium of the iris, without any definite mass formation.

In eye 7 R, in which the clinical reaction was greatest, the granuloma was largest and pro-

truded into the anterior chamber about one-third the distance across and extended, to a lesser depth, around the entire circumference of the angle (fig 1).

In the series of iridectomies, the foreign body tissue reaction bridged the coloboma in eye 1 R. In eye 3 R fibrous tissue was laid down at the site of iridectomy, although there was no complete bridging of the coloboma. In eye 9 R, the control, there was no evidence of foreign body giant cells or of fibrous tissue formation of any



Fig 4 (eye 7R)—Talc crystals in a foreign body granuloma in the anterior chamber. A indicates talc crystals and B, polymorphonuclear leukocytes.  $\times 200$

kind. This is in accordance with the observations of Daniel,<sup>7</sup> who showed that there was no permanent regrowth of iris or fibrous tissue following iridectomy in the rabbit's eye.

In the studies on submuscular injection, gross dissection revealed definite adhesion of muscle to sclera at the site of the granulomatous masses. Microscopically, these masses showed the same histologic structure as the granulomas in the anterior chamber.

In evaluating the practical significance of these reactions, one might ask how much talc can actually get into the tissues with the usual operative procedures. The answer is that as long as there is a possibility that any can get in, the danger should be avoided.

In surgical procedures on muscles, especially, the operative field is widely exposed in contrast to intraocular operations, such as cataract extraction, which in most instances are done through a small wound.

In surgical procedures for glaucoma, such as trephination, sclerectomy and other types of

7 Daniel, R. K. Healing of the Iris in Rabbits Following Experimental Iridectomy, *Arch Ophth* 31:292-298 (April) 1944.

filtering operations, it is easily conceivable that some talc may fall over the site of sclerectomy, or at the areas of inclusion of the iris. Certainly, it would be undesirable to have a foreign body granuloma formed at such a site. A granuloma here may easily occlude the tiny openings on whose patency depends the success or failure of the operation.

In muscle surgery, one is prompted to investigate the granulomatous masses often seen for many weeks at the site of operation. Perhaps one should have more proof before ascribing these masses to the type of suture material used or to the amount of resection, because it is conceivable that some of them might be foreign body granulomas produced by talc. It would be worth while to investigate such masses histologically.

To remove powder from gloves, it is best to have the assistant play the stream of saline solution from an irrigator over the operator's gloved hands before he starts working. The use of the irrigator for this purpose avoids the need for frequent change of the solution of mercury bichloride or cresol in the basin and assures one of a constant stream of clean saline solution, instead of one contaminated by the preceding surgeon's talc washings.

In the recent literature, there has been a good deal of discussion on various substitutes for talc. The two substances most favorably received thus far are potassium bitartrate<sup>8</sup> and hydrolyzed starch.<sup>9</sup> The potassium bitartrate is supposed to be rather easily absorbed by body fluids, instead of causing foreign body granuloma. Neither substance was easily available during the period of the war. Certainly, one of these, or, perhaps another substance, will be found to be a satisfactory substitute for talc. Before the new powder is adopted for use in surgical procedures, however, it would be well to carry out studies similar to those described with talc.

#### SUMMARY

Talc has been demonstrated to produce granulomas in the eyes of rabbits. When rubber gloves are used, it is advisable to remove all the talc before operating.

1840 Grand Concourse

8 Seelig, M. G., Verda, D. J., and Kidd, F. H. Talcum Powder Problem in Surgery and Its Solution, *J. A. M. A.* **123** 950-954 (Dec 11) 1943.

9 Seelig, M. G. Dusting Powder for Surgical Gloves, *J. A. M. A.* **125** 1208 (Aug 28) 1944.

# SCLERAL FLAP INCISION WITH SCLERAL SUTURES FOR THE CATARACT OPERATION

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MINNEAPOLIS

Ophthalmologists have given much time and thought to the perfection of the cataract operation. A considerable literature on the technic of cataract surgery has accumulated in recent years, much of it concerning accurate and firm closure of the incision.

It has been generally accepted that firm closure of the cataract wound leads to fewer postoperative complications, such as prolapse of the iris and vitreous, fewer cases of delayed closure of the anterior chamber and a considerable decrease in the incidence of postoperative hyphema. The experimental studies of Hilding<sup>1</sup> and the statistical studies of Leech and Sugar<sup>2</sup> and McLean<sup>3</sup> all bear this out. Firm closure of the incision allows the patient much more freedom of movement and permits the aged patient to be out of bed forty-eight hours, or even as early as twenty-four hours, after the operation. It is evident that this is quite an achievement when one considers the weakening effect of a prolonged stay in bed. Furthermore, postoperative astigmatism is found to be at least a full diopter less than when no sutures are employed.

Because of ease of application, the method of conjunctival suture introduced by Williams,<sup>4</sup> in 1869, finds many adherents. Especially is this true of ophthalmic surgeons who feel that the presence of a preplaced suture, particularly the corneoscleral suture, might interfere with the

making of a good incision. However, the conjunctival suture, while it is of definite value, offers the patient and the surgeon little more in the way of security than does no suture at all.

Recently the corneoscleral suture has become more commonly employed.<sup>5</sup> This suture, first introduced by Kalt<sup>6</sup> in 1894, with its various modifications since that time, is designed to be placed before the cataract incision is made. As its name implies, it consists of two parts, the corneal and the scleral, between which the cataract knife or keratome must pass in making the incision.

There are several drawbacks to use of the corneoscleral suture. If the corneal and the scleral part are placed close together, with an interval of 0.5 mm, as recommended by Kalt, it definitely interferes with the making of the incision. I have observed that the corneal and the scleral part of this suture are more likely to be placed 2 to 3 mm apart, in which case the lips of the wound are less firmly and less accurately brought together. Tying the suture too tight in such a case invariably causes inversion and buckling of the lips of the wound. Further, the wound is not well covered with conjunctiva unless a Kuhnt conjunctival flap is first made and sutured over it.

McLean,<sup>3</sup> in 1940, described a corneoscleral suture which he places through a groove made at the limbus under a small conjunctival flap. This suture overcomes the aforementioned drawbacks, except that it requires the utmost accuracy to pass the Graefe knife between the lips of the groove and, at the same time, to avoid cutting the suture. Even if one uses the keratome and scissors for making the incision, the suture may easily be severed.

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This paper was presented in moving picture form before the Forty-Ninth Annual Meeting of the American Academy of Ophthalmology and Otolaryngology, Chicago, Oct 10, 1944.

1 Hilding, A. Efficiency of Various Wound Closures in Prevention of Prolapse of the Iris After Cataract Operations. Experimental Study, *Arch Ophth* **22** 177 (Aug) 1939.

2 Leech, V. M., and Sugar, H. S. Reduction of Postoperative Complications in Cataract Operations with Corneoscleral Sutures, *Arch Ophth* **21** 966 (June) 1939.

3 McLean, J. M. A New Corneoscleral Suture, *Arch Ophth* **23** 554 (March) 1940.

4 Williams, H. W. Cataract Extraction Operations, *Arch Ophth* **1** 98, 1869.

5 Ellett, E. C. Use of Suture in Extraction of Cataract, *Arch Ophth* **17** 523 (March) 1937. Stal-lard, H. B. A Corneoscleral Suture in Cataract. Its Technique and Advantages, *Brit J Ophth* **22** 269, 1938. Verhoeff, F. H. A Corneoscleral Conjunctival Suture in Operations for Cataract, *Tr Am Ophth Soc* **25** 48, 1927. Walker, C. B. Exactly Appositional Sutures in the Cataract Operations, *ibid* **27** 51, 1929.

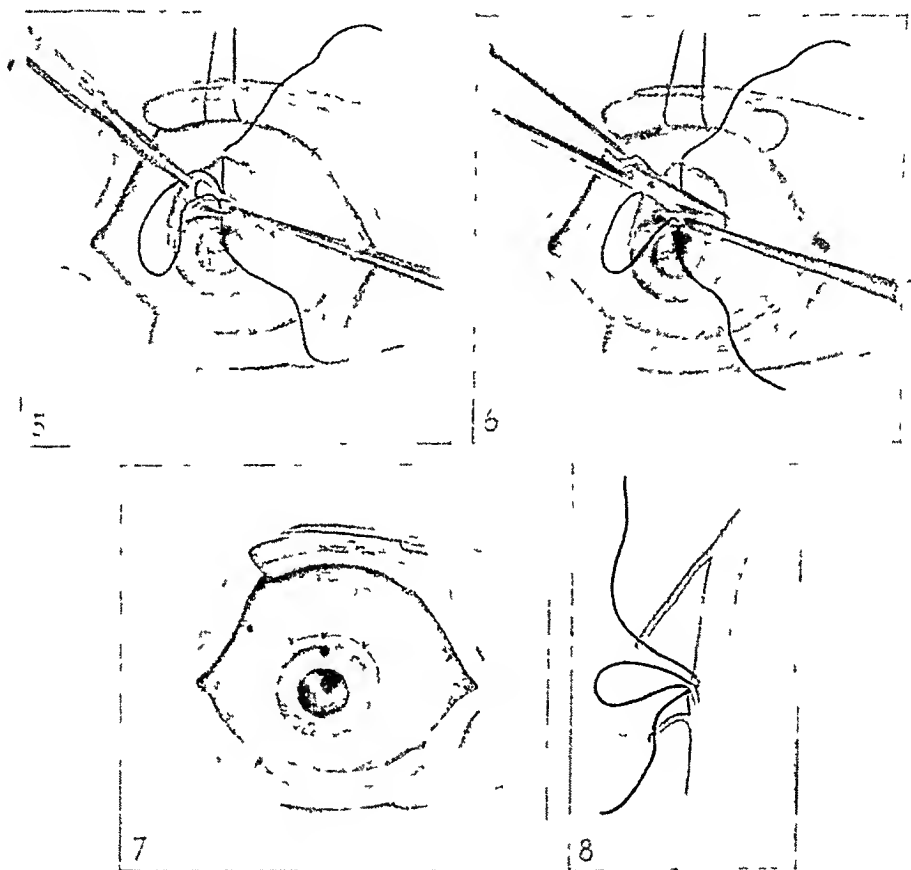
6 Kalt, E. On the Corneal Suture in Cataract Extraction, *Arch Ophth* **23** 421, 1894.

aside to permit the making of the incision (figs 2 and 3)

When the scleral flap is turned downward toward the cornea, an interval of 1.5 to 2.5 mm is created between the two parts of the suture, the size depending on the height of the scleral flap. This leaves ample space for the cataract knife to pass, without the risk of cutting the suture. For additional accuracy, however, I prefer to use the keratome and scissors in making the incision. Fixation of the eyeball is secured by grasping the scleral flap with a toothless conjunctival forceps, and the keratome is placed in

scleral flap is fixed and held away from the eye. The scleral knife now continues the incision into the anterior chamber (fig 5). The pressure exerted by the scleral knife is exactly countered by the traction with the forceps on the scleral flap, therefore there should be no prolapse of iris into the wound. The incision is now enlarged with scissors.

If, in the process of making the scleral flap, the anterior chamber is inadvertently opened and a prolapse of the iris occurs, the iris is replaced and the scleral suture is taken with almost the same ease as with an intact eyeball. However



Figs 5-8—5 illustrates an *ab externo* incision. The Lundsgaard scleral knife, in place of the keratome, is used to enter the anterior chamber.

6 shows enlargement of the cataract incision by means of scissors.

7 shows closure of the wound after the cataract has been extracted. The scleral suture has been tied tightly, and two auxiliary conjunctival sutures have been taken.

8 is a diagrammatic representation of the suture, which has passed through the conjunctival flap below the tip of the scleral flap, the upper lip of the sclera and the conjunctiva, above.

the groove at the base of the scleral flap (fig 4). The keratome is made to enter the anterior chamber, and the incision is enlarged with Stevens' scissors (fig 6).

Should the anterior chamber be very shallow, as in a case of glaucoma combined with cataract, an *ab externo* incision may be made. In such a case one may use a Lundsgaard knife in place of the keratome. With the suture in place, the

the upper lip of the scleral wound is fixed with a fine-toothed straight iris forceps in order that no pressure be exerted on the eye while the needle is being passed through the upper scleral lip. The opening in the anterior chamber is enlarged with scissors and the incision completed.

On completion of the extraction, the scleral suture is firmly tied, and two or more auxiliary conjunctival sutures are placed (fig 7). Figure



LAW OF PHYSIOLOGIC AGING AS DERIVED FROM LONG RANGE DATA ON REFRACTION OF THE HUMAN EYE

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FORMER RESULTS AND PROBLEMS

In former papers by one of us (F B)<sup>1</sup> and by his collaborators Steinhaus<sup>2</sup> and Heidemann<sup>3</sup> it has been shown that a statistical correlation exists between the development of presbyopia, i e, loss of the power of accommodation due to aging, on the one hand, and the span of life on the other. Statistically speaking this means that persons with early progressing presbyopia die early and that persons with late progressing presbyopia die late. Furthermore, by securing death records in a considerable number of cases (about 1,000) it was clearly demonstrated in the work of Steinhaus<sup>2</sup> that the correlation just mentioned is due primarily to the large subgroup of cases in which "apoplexia" or "heart stroke" (chiefly occlusion of the coronary arteries) was registered as the cause of death.

These former observations are demonstrated in tables 1 and 2.

The life expectancy of men and women who died of apoplexy or "heart stroke" for three classes of presbyopia is shown in table 1.

The column headed "Normal Presbyopia" includes the cases of persons whose presbyopia, measured by the addition for near vision, was found to be equal to the average with a margin of  $\pm \frac{1}{8}$  D. All persons with presbyopia of a

degree higher than average were classified as having "supernormal presbyopia" and those with presbyopia of a degree lower than normal were said to have "subnormal presbyopia."

The statistical facts presented in tables 1 and 2 indicate that aging in man must follow certain definite physiologic laws. The exact nature of

TABLE 1—Life Expectancy for Three Classes of Presbyopia of Persons Whose Cause of Death Was Arteriosclerosis\*

Age Group	Life Expectancy in Years		
	Supernormal Presbyopia	Normal Presbyopia	Subnormal Presbyopia
40-43	20.7 (33)	26.7 (61)	
44-49	17.9 (86)	22.5 (83)	31.8 (84)
50-53	15.5 (51)	18.9 (84)	23.2 (31)
54-58	11.2 (29)	13.9 (26)	19.8 (15)
59-63	11.4 (43)	10.3 (14)	13.4 (23)
64 and over	6.4 (22)	9.9 (41)	10.9 (44)

\* The number of cases is shown in parentheses.

TABLE 2—Average Life Expectancy for Three Classes of Presbyopia of Persons of All Age Groups with Different Causes of Death (Bernstein 1937)\*

Causes of Death	Life Expectancy in Years		
	Supernormal Presbyopia	Normal Presbyopia	Subnormal Presbyopia
Arteriosclerosis	15.0 (264)	19.5 (259)	22.2 (237)
Cancer	13.0 (47)	11.4 (34)	12.8 (38)
Tuberculosis	11.9 (42)	10.8 (35)	10.8 (26)
Grip	15.6 (63)	14.3 (40)	13.7 (62)

\* The number of cases is shown in parentheses.

This study was made with the support of a grant from the Council for Research in the Social Sciences of Columbia University.

1 Bernstein, F. (a) Alterssichtigkeit und Lebenserwartung, *Forsch u Fortschr* 8 272-273, 1932, (b) Die natürliche Lebensdauer des Menschen und ihre statistische und individuelle Beurteilung. Comitato italiano per lo studio dei problemi della popolazione, Rome, Istituto Poligrafico dello Stato Libreria, 1932, (c) Biologische Faktoren der Verminderung der Sterblichkeit, *ibid*, 1932.

2 Steinhaus, H. Untersuchungen über den Zusammenhang von Presbyopie und Lebensdauer, unter Berücksichtigung der Todesursachen, *Arch f Augenh* 105 731-760, 1932.

3 Heidemann, R. Presbyopie und Lebensdauer, *Inaug Dissert*, Göttingen, 1932.

these laws, however, could not be revealed by these statistical studies, which were based on data not giving information on the gradual development of presbyopia in the individual case. Our present paper abandons this statistical approach and deals with the nature of the laws which govern the gradual development of presbyopia in the individual case.

NATURE OF THE DATA

The present study is based mainly on data from the histories in 3,000 cases from the files of

Dr John E Weeks, former head of the department of ophthalmology, New York University. These data became available through the courtesy of Dr Webb Weeks, late head of the department of ophthalmology, New York University. The patients had been under observation for periods ranging from six to forty years, covering the period in which presbyopic changes take place.

In these 3,000 cases, all records were discarded in which the patient showed lower visual acuity. Data in all cases of cataract and, later, of glaucoma were considered only for the earlier, normal, years. All cases were excluded in which refraction seemed to be affected by general disease. Particular care was taken to eliminate all cases of diabetes. Cases of myopia in which there was a tendency to an increase in myopia during the period of observation were also discarded. Even in the category of constant myopia we retained only cases in which the myopia did not exceed  $-1.5$  D.

It soon became evident that the period of presbyopia to be studied had to be decidedly longer than six years if conclusive quantitative results pertaining to gradual development were to be obtained. Therefore, only the cases were used in which the presbyopic period covered at least twelve years. In addition, this period had to include at least six observations in each individual case.

Of the 3,000 cases collected, 344 satisfied these strict requirements. In each of the observations, the glasses prescribed fully corrected the vision to normal, so that the visual acuity was 20/20 according to the Snellen test. Whenever there was reason to assume a change in the reading distance, a corresponding correction was made, or the data were discarded. The logical continuation of the work by Steinhaus and Heidemann on presbyopia would have been a study of the changes in power of accommodation with age in single subjects. Such a study requires observations made especially for that purpose. Data from prescriptions on the other hand, are the only ones available in sufficient numbers for a study of the development of refraction in individual subjects, with the necessary extension over long periods.

All three elements of the prescription, namely, the sphere for distance, the astigmatic correction by a plus or a minus cylinder and the correction for near vision, change with age.

The corrections prescribed have two purposes: to enable the patient (1) to read at the distance of 6 meters and (2) to read with ease standardized print at a convenient reading distance.

Since for most patients of presbyopic age the second correction is the more important, and since it includes the elements of refraction studied by Steinhaus and Heidemann, we decided to study the development of refraction with regard to the correction for near vision, with elimination, however, of the correction for astigmatism, since astigmatism may develop according to laws of its own.

The total refraction of the reduced eye of Listing (one medium) consists of the sphere which osculates the refracting surface and a hyperboloid surface of Gaussian curvature zero, which is approximated by a crossed cylinder. The osculating sphere is corrected by a sphere whose dioptric strength is the sum,  $y$ , of the sphere for distance, the addition for near vision and half the diopters of the correcting plus cylinder minus half the diopters of the correcting minus cylinder. The crossed cylinder is corrected by a crossed cylinder,  $C$ , with opposite signs of the two curvatures. The crossed cylinder  $C$  consists of two crossed cylinders, of which the first has half the strength of the plus cylinder and the second, placed at right angles to the first, has half the strength of the minus cylinder. This separation of the correction remains valid also for the eye with several diffracting media.

This separation of the correction into the sum  $y$  and the crossed cylinder  $C$  is merely formal. But since Wibaut<sup>4</sup> has shown statistically that the two radii of curvature of the cornea change with age in opposite directions exactly the same amount, so that the middle value remains unchanged with age, it is to be assumed that the astigmatism of the cornea is described by a changing crossed cylinder. Apparently the cornea changes with age by being bent in the vertical direction without any kind of deformation<sup>5</sup> so that the increase of curvature in the one principal section is accompanied with an equal decrease of curvature in the other.

Stern and Rosenberg<sup>6</sup> conducted a study of astigmatism in the 3,000 cases on the basis of the ophthalmometric readings and the subjective and objective determinations of astigmatism always made for each new patient. They showed statistically that the axis of the lenticular astig-

4 Wibaut, F. Biologisch-statistische Refraktionsuntersuchungen, Munich, J. F. Bergmann, 1932.

5 This entails the constancy of the geometric mean of the radii, but since the difference of the radii is small their arithmetical mean will also remain practically constant.

6 Stern, C., and Rosenberg, H. The Relative Contribution of Cornea and Lens in the Changes of Astigmatism with Age, Thesis, New York University, 1940.

matism remains unchanged with age. This suggests that the process underlying the change of astigmatism of the lens, whenever it occurs, will hardly add to or subtract from the spherical refraction.

One must conclude, therefore, that it is reasonable to expect that the processes underlying the change in the total spherical correction for near vision,  $y$ , and the processes underlying the change of the crossed cylinder,  $C$ , act so that the first processes change sphere in sphere and that the second processes change crossed cylinder in crossed cylinder. In studying the development of  $y$ , we therefore assumed that we had eliminated the influence of all processes causing changes of astigmatism with age. An illustration of this situation could be seen in a case in which the refraction of the two eyes was the same from 40 to 51 years of age but in which astigmatism continued to develop in the right eye while in the left eye a weak astigmatism, such as had existed in equal degrees in the two eyes, remained unchanged. During the whole subsequent period of observation, extending from the age of 51 to that of 73½ years, prescription for the right eye and that for the left differed only by the addition of a crossed cylinder for the right eye. This crossed cylinder was apparently the true expression for the change in astigmatism of the right eye. There were other cases of a similar, but less striking kind, and no case was found which contradicted the theoretic assumption made here.

It will be noted that the processes involved in the development of  $y$  are two: first, the senile increase in hypermetropia and, second, the decline of the power of accommodation. It will be seen later that these two processes are closely related and that they can be traced back to a common cause (see "Comment").

It may be stated in advance that for the study of the process of aging the analysis of  $y$  offers one great advantage. The value for  $y$  undergoes changes in development far past the age of 60, at which age the addition for near vision in usual practice attains a final value. In the data of Dr. Weeks the final value of the addition in most cases is already attained at the earlier age of 55. This constituted an additional reason for concentrating on the study of the total spherical correction,  $y$ , for near reading.

#### GRAPHIC REPRESENTATION OF THE DATA

All data on long range development have been plotted on coordinate paper, as illustrated in case 143 (fig. 1). The symbols used are self explanatory.

We have tried to interpolate graphically and numerically the values for the total correction,  $y$ , as a function of age through the equation

$$(1) \quad y = A [1 - 2 - (\tau - \tau_0)/c]$$

This has been done with the aid of semilogarithmic paper, to which the bases 2 in formula 1 refers. The value for  $y$  is measured in diopters, and  $\tau$ , in 10 year units. For each eye the value  $A$ , called an asymptote, was determined at first by trial and error,  $A$  being varied so that the points representing the values for  $A-y$  were finally lying close to a straight line on semilogarithmic paper (fig. 2, case 143). This yields an angle,  $\alpha$ , between the upper part of the

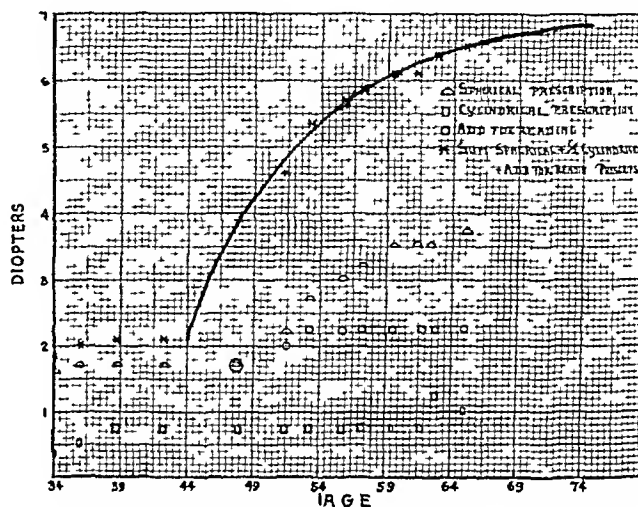


Fig. 1—Graph showing corrections prescribed for the right eye of a patient (case 143) with presbyopia under treatment over a period of thirty years.

straight line and the  $\tau$  axis to the left of it, the cotangent of which is  $C$ . The constant  $\tau_0$  is the

7. In the corrections the development of which is studied here, the distance of the lens from the eye enters as an unknown, variable quantity. In case this distance is recorded, which was not done in our data, that value should be used to calculate the true refractions and to determine  $A$  and  $c$  from them. This, of course, still requires an assumption about the distance of the first principal point from the surface of the eye.

In order to illustrate what changes would occur if true refractions were used, the distance of the lens from the surface of the eye is assumed to be 12 mm and the distance of the principal point from the surface of the eye 135 mm, in accordance with Gullstrand. In case 143, for example, we obtained  $A = 7.70$  instead of  $A = 7$ . But  $c$  remained wholly unchanged.

In fact, the true refractions are proportional to the corrections belonging to a given distance of the lens from the eye, with a factor of proportionality which is fairly constant within the limits of refractive changes occurring during presbyopia. Therefore the formula 1 with the same  $c$  but a different  $A$  fits corrections as well as the true refractions in an individual case.

age at which the ordinate of the straight line is equal to  $A$ . In the first diagram (fig 1),  $y$  would be zero if the curve could be prolonged backward until it cut the  $x$  axis.

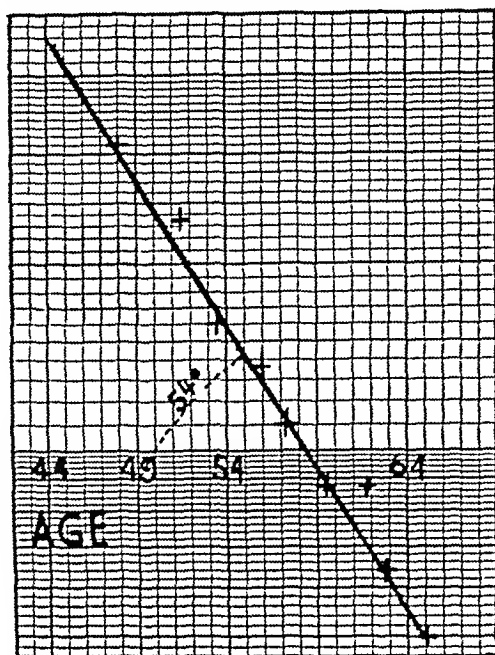


Fig 2—Values for  $A - y$  (formula 1) for the right eye in case 143, plotted on semilogarithmic paper. The plus sign indicates asymptote  $A (= 7 D)$  minus sum  $y$ .

In case 143 (fig 1) it can be observed that up to the age of 42 years  $y$  remains almost constant. After that age the correction for distance

more general method for three nonequidistant ordinates requires the solution of a trinomial equation with irrational exponents. Such a direct determination of  $A$  was worked out, and tables were calculated. This procedure will be published elsewhere.

#### FIT OF THE FORMULA

The accuracy of determination of the spherical correction is  $\frac{1}{8} D$ , and in correction for near vision it is seldom more than  $\frac{1}{4} D$ , so that the accuracy of determination of  $y$  lies somewhere between  $\frac{1}{8}$  and  $\frac{1}{4} D$ .

Table 3 is so arranged that each point deviating more than  $\frac{3}{8} D$  from the corresponding point of the straight line is listed three times—as deviating more than  $\frac{1}{8} D$ , as deviating more than  $\frac{1}{4} D$  and as deviating more than  $\frac{3}{8} D$ , from the value on the line. As the survey shows, the number of points deviating more than  $\frac{1}{8} D$  appears small when the accuracy of the determination of  $y$  is taken into account. The number of points deviating more than  $\frac{1}{4} D$  is still smaller, and the number of points deviating more than  $\frac{3}{8} D$  appears very small and, when checked, is found to be attributable mainly to discontinuous changes in correction for near vision.

TABLE 3—Goodness of Fit Sample of 10 Cases\*

Age Interval of Observa tion, Yr	No of Observations with Deviations in Diopters of More Than														
	Asymptote		Angle Alpha		Age X <sub>0</sub>		No of Points (n - 3)	Right			Left				
	Right	Left	Right	Left	Right	Left		1/8	1/4	3/8	1/8	1/4	3/8		
40-70½	4.62	4.62	46.5	46.5	47½	37½	7								
42-69	4.88	5.25	50	50	42½	42	5	2	1						
28-59½	5.50	4.88	50.5	50.5	37½	37½	6	2	1						
39-57	5.00	5.00	55.5	55	36½	36½	7	1	1						
36-55	5.75	5.75	63	63	41¾	41¾	4	1	1		1				
35-64½	5.75	5.25	58	58	38½	38½	5	1	1		1		1		1
44-58	6.50	5.75	49	50	38½	38½	5	1			1				
34-61½	4.50	4.62	51	51	36½	36½	5	2	1		1				
38-63	4.75	4.75	56	56	36	36	7	2					1		
47-67	4.38	4.38	55	55	42½	42½	6	1					1		

begins to rise and, at about the same time, the addition for reading does also. The astigmatism remains constant throughout.

The trial and error method of determining  $A$  is fairly accurate, but the following numerical method proved finally superior. From any set of values of  $y$  given for three successive equidistant values of  $x$ ,  $A$  can be determined by the following rational formula, first developed by J. Lipka:

$$(2) \quad A = y_1 + \frac{(y_2 - y_1)^2}{2y_2 - y_1 - y_3}$$

The application of this formula requires generally the calculation of  $y_2$  through interpolation in order to have three equidistant ordinates. A

#### FIRST (GLOBAL) STATISTICAL TEST OF THE EXPONENTIAL LAW OF AGING

A similar test is given in table 4 for 400 eyes. The cases are grouped according to the reduced number of prescriptions ( $n-3$ ) derived from the individual cases. This table shows that the more observations for a single eye, the more accurate is the determination of the three constants of the curve which expresses the development of the refraction, and therefore the more satisfying is the representation. In fact, in 115 cases with 8 or more observations each, covering a period of twenty-two and eight-tenths years in which the most pertinent check could be made,

only 10 per cent of the observations were found with deviations of more than  $\frac{1}{4}$  D. The deviations in this 10 per cent of cases were mostly attributable to discontinuous changes in the prescription for near vision.

If the index,  $y$ , of total refraction develops according to a general aging process, no difference in the trend of aging between the right and the left eye is to be expected. This conclusion, indeed, has been confirmed except only in cases in which the condition was manifestly pathologic.

It sufficed, therefore, in plotting the data in a case to use only one eye, preferably the one with the greater visual acuity. But it was of interest to note that the two eyes, although having equal trends, expressed by  $c$ , differed frequently with regard to the asymptotic value of the total refraction.

but

$$(4) \quad A' = A 2^{-(s_0 - r_0)/c}$$

which results from

$$a' = A [1 - 2^{-(s_0 - r_0)/c}]$$

$a'$  being the value of the sum  $y$  at the time,  $s_0$ , age of onset of presbyopic changes. Accordingly, the straight line in the semilogarithmic plane representing equation 1 represents also equation 3.

Our first test of linearity made use of both eyes of a subject, as though they represented independent observations. The deviations from the straight line in the logarithmic plane are composed of those originating (a) from the spherical correction for distance, (b) from the cylinder and (c) from the addition for near vision. Of these deviations, the last are normally always identical for the two eyes, while the deviations for (a) and (b), resulting from independent examination, vary independently. The

TABLE 4—Goodness of Fit of Curve 1  $y = A [1 - 2^{-(r - r_0)/c}]$

Eyes Grouped According to Reduced Number of Points (n - 3)*	Number of Observation Eyes	Reduced Number of Observation Points	Average Age at First Prescription, yr	Average Age at Last Prescription, yr	Average Duration, yr	(a) Reduced Number of Observation Points (b) Reduced Number of Observation Points, in Percentages With Deviations from Curve 1		
						Less Than 1/8 D	Between 1/8 and 1/4 D	More Than 1/4 D
						(a) 122 (b) 59.60	(a) 45 (b) 22.67	(a) 36 (b) 17.73
1 and 2, inclusive	115	203	44.30	61.04	16.74	(a) 360 (b) 60.71	(a) 133 (b) 22.43	(a) 100 (b) 16.86
3 and 4, inclusive	169	093	41.30	63.78	22.30	(a) 484 (b) 69.34	(a) 131 (b) 18.77	(a) 83 (b) 11.89
5 and above	115	693	42.97	65.77	22.80	(a) 906 (b) 63.77	(a) 309 (b) 20.77	(a) 216 (b) 15.46
Total	399	1,494	43.78	64.33	20.55			

\* Number of observed points minus 3 points

This difference as a rule was present at, and even before, the moment when the curve of total refraction started to rise and then remained constant throughout the whole course of the later development. If the amount of total refraction at the age of onset of presbyopia is indicated by  $a'$ , the formula for total refraction as a function of age  $r$  for each eye is then

$$(3) \quad y = a' + A' (1 - 2^{-(r - s_0)/c})$$

where  $s_0$  is the age of onset of the presbyopic change,  $a'$  being positive for persons found to be hypermetropic and negative for persons found to be myopic at the time,  $s_0$ , of onset of the presbyopic change. Thus,  $a'$  is different for the two eyes while  $s_0$ ,  $A'$  and  $c$  are the same for the two eyes. As an example, we cite case 58 (figs 3 and 4). The difference in  $a'$  between the two eyes amounts to 1 D.

It is perhaps not superfluous to emphasize that the two equations 1 and 3 are valid at the same time. We have, therefore, not only

$$A = A' + a'$$

values of  $y$  belonging to the points on the two straight lines, however, are nearly identical for the two eyes, because both represent the trend of aging in the same subject.

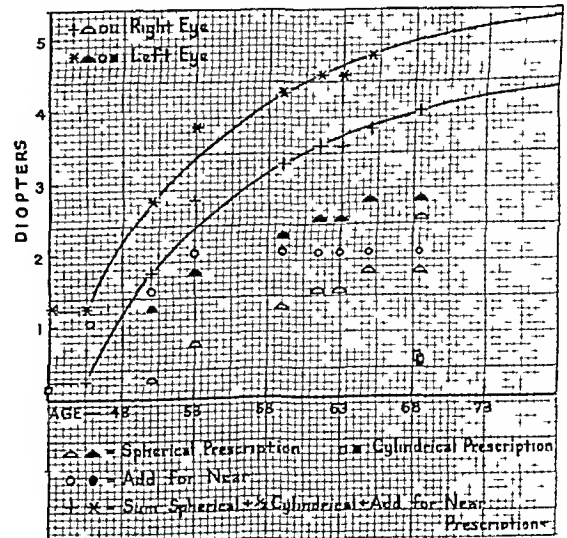


Fig 3—Curves for total refraction as a function of age  $r$  for each eye in case 58 as expressed by formula 3



In testing the linearity we first tried to combine the data for the two eyes, using, however, the addition only once, but it proved to be more profitable to use one eye only, preferably the one with the greater visual acuity. An elaborate combination of the data from the two eyes in each case could be dispensed with as long as an increase in the number of cases yielded improvement of the test to any desired accuracy. In this way, a test of linearity of the logarithmic graph, using only independent observations, was made for each eye of 200 subjects. The results of the tests are shown in tables 5 and 6.

TABLE 5—Test of Linearity of the Straight Line on Semilogarithmic Paper for 200 Subjects, Using Three Points of the Eye with the Best Visual Acuity

Diopters, Each Eye	Residual Points
0 1/8	506
1/8 2/8	153
2/8 3/8	29
3/8 and more	16
Total	704

TABLE 6—Percentages of Residual Points for the Two Eyes

	0 1/8 D	1/8 2/8 D	2/8 3/8 D	3/8 D and More
Eye with best visual acuity	71.97	21.73	4.12	2.27
Other eye	65.03	21.84	7.93	5.20
A tentatively formed weighted average gives percentages	60.00	21.74	5.72	3.45

The accuracy of determination of distance vision lies between  $\frac{1}{8}$  and  $\frac{1}{4}$  D. We believe that the 45 and 704 deviations beyond  $\frac{2}{8}$  D are not representative of the actual state of vision. We found that they were due mostly to relatively high changes in the addition. In some cases the deviation seemed to be due simply to contradictory statements of the patients, as judged from the records, since the patients then returned after shorter intervals than usual. In a few other cases the oculist may have had a reason for giving temporarily either more or less corrective glasses. In 37 out of 179 cases the first prescriptions were too strong, and in 4 cases they were too weak, to be in accordance with the linear graph. In such cases the first prescription was not used in determination of the linear graph.

The small number of the deviations beyond  $\frac{2}{8}$  D does not indicate in any way chance variation, and therefore we did not apply statistical routine procedure for determination of the best fitting straight line but proceeded graphically, selecting the three points which, according to judgment, seemed the best choice for leading

to a straight line representing the total trend. The 200 cases indicated in tables 5 and 6 were those with the relatively greatest number of observations, leading thus to the most significant test of linearity.

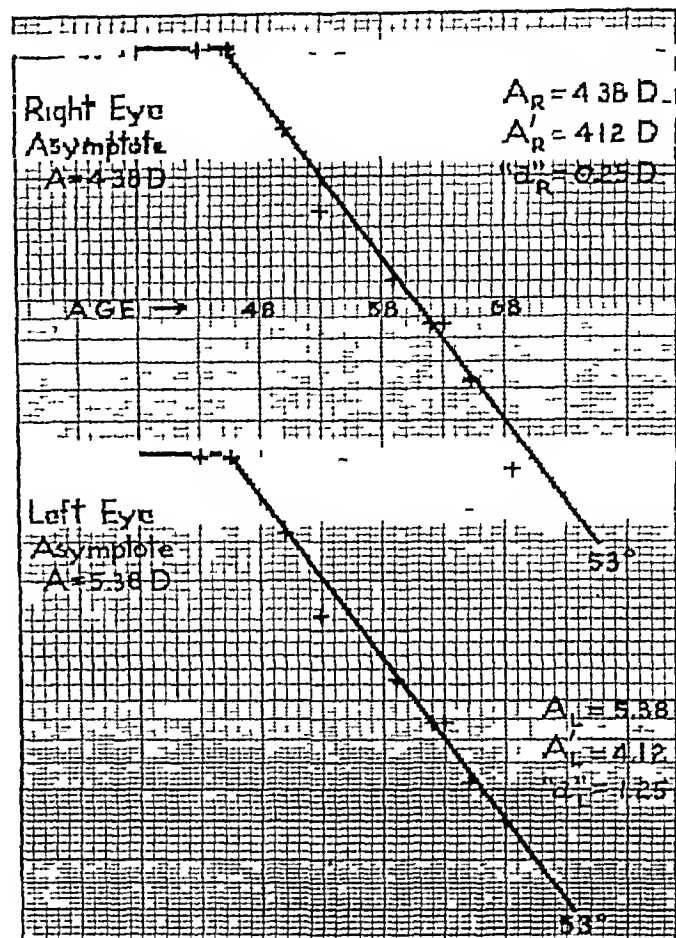


Fig. 4—Values for  $A-y$  for each eye in case 58, plotted on semilogarithmic paper

But the 143 cases of presbyopia of shorter duration also confirm the law, as seen in table 7.

TABLE 7—Test of Linearity of the Straight Line on Semilogarithmic Paper for 143 Subjects, Using Three Points of the Eye with the Best Visual Acuity

Diopters, Each Eye	Residual Points
0 1/8	664
1/8 2/8	223
2/8 3/8	81
3/8 and more	53
Total	1,021

For 60 cases in which enough values for presbyopia were given for the determination of an asymptote, the average difference between the angle  $\alpha$  of the straight line, representing the development of the addition for near vision, and the line representing the development of the total index of refraction (sum  $y$ ) was found to be only  $1.008^\circ$ . The law of linearity is valid for both sexes. Whether or not a sexual difference exists in the constant of the linear law will be discussed later. No change of trend at any pair-



ticular age, such as that of the menopause, has been found

PREDICTION OF LATER DEVELOPMENT OF  
REFRACTION FROM KNOWLEDGE OF  
THE PRESCRIPTIONS OF AN  
EARLIER PERIOD

An interesting application of the law of aging is the possibility of using it for prediction of later development of refraction. For such a study we selected 80 cases in which the age interval from 10 to about 65 years or more was covered by a sufficient number of points of observation. The index,  $y$ , of physiologic aging at the age of 65 for these cases was calculated in two ways. First only 4 or 5 of the earliest observations were plotted, and from these the preliminary asymptote was determined graphically on semilogarithmic paper and numerically with the aid of the formula

(2)  $A = y + \frac{(32 - 31)^2}{2 \cdot 32 - 31 - 33}$

Thus the straight line on semilogarithmic paper was drawn, and from it the preliminary angle alpha and the value of the index at the age of 65 were determined by extrapolation, the result constituting the predicted value at the age of 65.

TABLE 8—*Prediction of Physiologic Age at 65 Years from First Four or Five Observations (10 Selected Cases)*

Case No		Asymp tote, D	Angle Alpha, Degrees	Index $y$ at 65 Yr, D	Age at First Observation	Age at Fourth (or Fifth) Observation	Age at Last Observation
286	Predicted	3.88	49	0.45	42¾	50½	66
	Observed	4.00	51	0.44			
326	Predicted	4.25	52	0.45	42¾	47¾	65
	Observed	4.38	51.5	0.47			
304	Predicted	7.00	51.5	0.33	37	46¾	62½
	Observed	7.00	51.5	0.33			
318	Predicted	2.88	47	0.48	42	53	68½
	Observed	2.88	47	0.48			
327	Predicted	8.00	51	0.80	43	52¾	62½
	Observed	7.62	56	0.55			
339	Predicted	4.75	54	0.57	46	56¾	69
	Observed	4.62	52	0.62			
341	Predicted	4.88	49	0.50	42	52	66¾
	Observed	4.62	50.5	0.43			
537	Predicted	4.62	52.5	0.60	45	55	73
	Observed	4.50	55	0.50			
289	Predicted	6.38	47	0.60	45	58	66½
	Observed	6.50	48	0.61			
292	Predicted	5.62	47	0.46	37	53¾	63¾
	Observed	5.50	48.5	0.43			

Second, the value of the index at the age of 65 if not given by direct observation, was determined by interpolation between or extrapolation from the nearest observations, the result constituting the "observed" value of the index at the age of 65.

Third, the angle alpha and the asymptote were always determined on the basis of all observa-

tions in order to obtain what we consider the true values of the angle alpha and the asymptote. The second determination, of course, includes the data of a case used in the first, but with comparatively small influence, in view of the long period of the observation.

TABLE 9—*Prediction of Physiologic Age at 65 Years from a Partial Period of the First Four or Five Observations (80 Cases)*

No. of Cases	Average Duration of Partial Period, Yr	Average Difference Between Predicted and Observed Values		
		Asymp tote A, D	Angle Alpha, Degrees	Index $y$ at 65 Yr of Age, D
20	5.75	0.131	2.925	0.100
20	8.53	0.119	2.025	0.070
20	10.45	0.163	2.725	0.115
20	14.0	0.094	1.300	0.071
Total 80	9.68	0.127	2.288	0.089

A comparison of the predicted index and the observed index, of the preliminary asymptote and the true asymptote and of the preliminary alpha and the true alpha angle show close agreement. The agreement between the "preliminary" and the "true" values is, at the same time, also an agreement between prediction and observation. We have tabulated the results of such a prediction for 10 cases chosen at random (table 8) and for the total series of 80 cases (table 9).

As the tables show, there was an average difference of only 0.127 D between the two values of the asymptote, an average difference of 2.288° between the two values of the angle alpha and an average difference of only 0.089 D between the predicted and the observed index at the age of 65.

THEORETIC CONSIDERATIONS

The simple law equation (1) for the development of  $y$  calls for casual explanation. Equation 1 may be written in the form

(5)  $A - y = A^2 - (x - x_0)/c$

The left side of formula 5 is the increase of the addition for near vision plus the increase of the true sphere for distance (corrected so that the astigmatism is eliminated).

As has already been mentioned, the relation between the two components of  $y$  varies with the amount of atropinization. Herrenheiser<sup>8</sup> advanced the hypothesis that the increase in senile hypermetropia is due to the gradual manifestation of undetected preexisting hypermetropia with increasing age. His theory is in agreement with modern experience as to the action of drugs.

8 Herrenheiser, J. Die Refraktionsentwicklung des menschlichen Auges, Ztschr. f. Heilk. 23: 342-377, 1892.

in samples of organisms. It has been shown that there exists such a wide variation of effect that there will be found in every large sample some organisms not affected by the drug. Straub and Falkenburg<sup>9</sup> found 6 cases in which atropine did not reveal hypermetropia in a sample of 59 subjects all of whom were in the twenties and were known to have been hypermetropic at an earlier age. The authors concluded that tectonic changes must have taken place. But in the light of recent pharmacologic experience such a conclusion does not seem well founded. Similarly, the conclusion that the increase in senile hypermetropia must be explained by tectonic changes because of the failure of atropine to reveal a pre-existing hypermetropia, as correctly postulated by Herrenheiser, seems, again, logically unwarranted.

In addition it is to be noted that the smooth muscles easily assume a state of semipermanent contraction which, according to Bethe,<sup>10</sup> can be sustained with little expenditure of energy. A semipermanent contraction, as described by Bethe, may not be sensitive to atropine at all. If this theory is accepted, the two components of  $A - y$  are both manifesting the power of the ciliary muscle to contract, and they constitute together the true power of accommodation at the age  $x$ . It has, then, to be explained further only why this power decreases exponentially.

The theory of accommodation proposed by Helmholtz in the form in which it is usually stated is not suited as a basis of explanation. The failure of this theory to account for the acceleration of the effect of atropine with age has been noted already by Duane.<sup>11</sup> The theory, however, as far as the kinematics of the mechanism is concerned, has been amply proved by Hess<sup>12</sup> and, recently, by Fincham.<sup>13</sup> Fincham presented proof that the capsule of the lens is the source of the capillary forces which round out the lens in accommodation, while the interior of the lens consists of inert matter in a semi-fluid state.

As Duane pointed out correctly, in the usual statement of the theory, the ciliary muscle spends an increasingly smaller part of its power in releasing the capillary action of the capsule of the lens, so that, contrary to experience atropine should paralyze the needed effort to a progressively less degree. The equation 5, as well as the experiments of Duane, requires that the ciliary muscle spend its full power in the act of maximal accommodation, as postulated in the theory of Tscherning. We have, therefore, modified the theory of accommodation proposed by Helmholtz in the following way:

The power of the ciliary muscle is increasingly absorbed in the action of contracting against the elastic resistance of the zonula-sclera system, which holds the lens in suspension. That the zonula is connected with the sclera by connective tissue, which, by-passing the ciliary body, can transmit the tension, is anatomically certain. The elastic resistance,  $R(1)$ , is assumed to increase according to an exponential law, and this explains the equation 5. It explains, also, why the effect of atropine is accelerated with age when the power of the ciliary muscle becomes largely absorbed by its action against the increasing elastic resistance,  $R(x)$ .

That the increase of  $R(1)$  with age is exponential conforms to the laws of colloid chemistry. The tissues of the body are colloid solutions, which desiccate with age in proportion to the water still present. This leads to the exponential law of decrease of water content of the tissues and, consequently, to the exponential increase of the constant,  $R(1)$ , of Hooke's law of elastic resistance, considered as a function of the age  $x$ . Measurements of the dry weight of various parts of the body have been made by Buerger and Schlomka (Bernstein<sup>14</sup>). They conform to a law of exponential increase with age.

In the foregoing explanation, the implicit assumption has been made that the nearly maximal contraction of the ciliary muscle assumed and sustained in accommodation for reading, decreases in proportion to the increase of the elastic resistance,  $R(x)$ , of the zonula-sclera system. Hill and Hartree confirmed the previous observations of Fick that in series of isometric contractions of striated muscle the length varies approximately in inverse proportion to the maximal tension, although there are some deviations from proportionality at either end of the scale. In the presbyopic period, hypertrophy of the ciliary muscle can be disregarded and the supposed inverse proportionality between tension and length can be assumed, in analogy to the

9 Straub, M., and Falkenburg, J. Ueber die normale Refraktion des Auges und die Hypertropie bei angeborener Amblyopie, *Arch f Augenh* **26** 336-362, 1892.

10 Bethe, A. Die Dauerverkürzung der Muskeln, *Arch f d ges Physiol* **142** 291, 1911.

11 Duane, A. Studies in Monocular and Binocular Accommodation, *Am J Ophth* **5** 865-877, 1922, Accommodation, *Arch Ophth* **5** 1-14 (Jan) 1931.

12 Hess, C. Die Refraktion und Akkommodation des menschlichen Auges und ihre Anomalien, in Graefe, A., and Saemisch, T. *Handbuch der gesamten Augenheilkunde*, Leipzig, W. Engelmann, 1910.

13 Fincham, E. F. The Mechanism of Accommodation, *Brit J Ophth*, 1937, supp 8, pp 5-80.

relationship observed in a series of isometric contractions of one and the same muscle

Further, we have assumed that the two step contraction of the ciliary muscle, namely, first from the resting stage to semipermanent equilibrium and then from that equilibrium to nearly maximal contraction, is dynamically equivalent to a one step contraction. This is approximately true, since, as Duane has observed, patients after atropinization may have lost for several months a small amount of their power of accommodation, so that the near point recedes somewhat, but they will still be able to accommodate nearly as much as before.

#### CONCLUSION

It has been the object of this paper to establish and explain the law of aging as revealed by the long range development of refraction.

This goal has been reached by elimination of questions interesting in themselves, such as the development of astigmatism and the respective developments of distance refraction and accommodation for near vision. For the establishment of the physiologic law as such, questions like a possible sex difference in aging may be disregarded and reserved for special studies.

The most interesting aspect of the result gained is that a method has been achieved by which one may determine fairly accurately a constant,  $c$ , which describes the exponential velocity of the change with age of the total spherical refraction of a subject.

In the biologic interpretation of the law, this velocity,  $c$ , is nothing else than the exponential velocity with which one tissue of the body changes from the sol stage to the gel stage. No assurance can be given that the other tissues of the body change with the same exponential velocity. But it is plausible that a correlation exists between the velocities of desiccation of the various tissues of the body with age. The results of Steinhaus and Heidemann with regard to a correlation between presbyopia and death from natural causes must be understood as based on a correlation between the velocities of desiccation of the various tissues of the body. The length of life is conditioned not only by internal but by external factors. In view of the large variation of the external factors of environment, this correlation must be rather great in order to express itself so clearly in the cited statistics.

It cannot be denied that considerable interest and prospect of basic clarification attaches to a study of such correlations in a direct manner, for which the way now seems to be opened. If it is desired to use immediately the results

here established for the purpose of general medicine, the way in which it can be done is evident.

The values of  $c$  derived from the 344 cases of presbyopia of long duration vary considerably. These values of  $c$ , or, better, the values of the angle  $\alpha$  of the logarithmic diagram, can be recorded in different classes, say, five classes, in which the values for the angle  $\alpha$  determined from the history of refraction can be recorded for each subject. This classification record, then, tells whether the person is aging normally, whether he is aging more rapidly than normal or whether he is aging more slowly than normal. With much greater reliability than the classifications of Steinhaus and Heidemann, such a classification would characterize the individual patient as an aging organism.

Although we have prepared such a table, we do not include them in this paper, for the reason that the 344 cases, selected on the basis of long duration, represent a biased sample. It is evident that such bias excludes the cases of presbyopia of short duration and, in consequence, the cases of quick and unfavorable aging. Our norm would lie at too high a level. We should classify too many cases in the most unfavorable category.

This deficiency of our classification might be corrected after we have learned the date of death of the 344 persons, most of whom have already died. The determination whether, with the evidence now at hand, and with a plausible allowance for the bias of our table, the diagnosis of the velocity of aging,  $c$ , from the history of refraction as presented here, may add to the knowledge of a basic age characteristic of an individual subject, with sufficient reliability to be of unmistakable significance for general medicine, is at present still in the experimental stage of trial and error.

#### SUMMARY

As reported in earlier publications by one of us (F. B.) and his collaborators Heidemann and Steinhaus, a statistical correlation exists between presbyopia, as measured by the gradual loss of power of accommodation, and the length of life. By securing death records in about 1,000 cases, Steinhaus showed that the correlation was due exclusively to the cases in which death was the result of arteriosclerotic changes. In 5,000 cases obtained from various sources, Steinhaus and Heidemann found no difference between men and women in the average amount of developing presbyopia. Neither was there any difference between the urban and the rural population or among different social classes.

The present study is summarized

1 From the files of Dr John E Weeks, former head of the department of ophthalmology of New York University, 3,000 cases were selected, in which the development of refraction and the changes in prescriptions could be followed through periods ranging from six years to over forty years, covering ages from 35 to the highest calendar ages. From these 3,000 cases were selected 344 in which presbyopia had been present more than twelve years and 6 or more prescriptions had been given. In none of these cases were there any pathologic traits or more than 1.5 D of myopia, and in all visual acuity was 20/20 in the Snellen test.

The refraction in each case, consisting of the spherical prescription for distance, the cylindrical prescription and the additional spherical prescription for reading distance was plotted against age.

2 The total refraction was represented by the sum of the following two independent optical components: (a) a sphere of the amount of the sum,  $y$ , of the spherical prescription for distance, the addition for near vision and half the strength of the plus cylinder prescribed for astigmatic correction, and (b) a crossed cylinder,  $C$ , the positive component of which was half the positive cylinder of the astigmatic prescription, with the same axis.

The laws of development for  $y$  and  $C$  are wholly independent of each other. Comparison of the results for the two showed that in individual cases the crossed cylinder,  $C$ , may develop differently for the right eye and the left eye, while the total spherical correction,  $y$ , may develop identically for the two eyes.

3 An attempt was made to represent the development of the sphere  $y$  by a curve according to the formula

$$(1) \quad y = A (1 - 2^{-(x-x_0)/c})$$

where  $x$  is the calendar age and  $A$ ,  $x_0$  and  $c$  are constants, determination of which requires the knowledge of three values of  $y$ , calculated for three different ages. The determination was first made with the aid of semilogarithmic paper, for which 2 is the base of the logarithmic system. The constant  $A$  was first determined by trial and error. Later, the following formula was used

$$(2) \quad A = y_1 + \frac{(y_2 - y_1)^2}{2y_2 - y_1 - y_3}$$

which is valid if the three ages,  $x_1$ ,  $x_2$ ,  $x_3$ , for which the  $y_1$ ,  $y_2$ ,  $y_3$  are calculated, follow each other at equal intervals. It is usually necessary to gain the  $y_2$  for the middle value by interpolation.

Tables for the determination of the constants for the more general case in which  $y$  is calculated

for three ages not following each other at equal intervals have been calculated.

4 For the test of goodness of fit of the formula (1), 1,494 observations, not used in the determination of the three constants, were available for 400 eyes belonging to the 200 persons with the maximum number of observations.

Of these 1,494 observations, 69.3 per cent were lying within the  $\frac{1}{8}$  D distance of the straight line of the semilogarithmic graph and 88.1 per cent within the  $\frac{1}{4}$  D distance. For 144 eyes with a lesser number of observations and a shorter period, 84.5 per cent of observations were lying within the  $\frac{1}{4}$  D distance of the straight line.

Because of the equality for the two eyes of the addition prescribed for near vision, a statistical dependence is created between the deviations used in the test. In the second test, in which this statistical dependence was avoided by using the data for one eye only, 72 per cent were found within the  $\frac{1}{8}$  D distance and 93.7 per cent within the  $\frac{1}{4}$  D distance for the 200 subjects.

5 An individual analysis of the relatively few cases represented by the 6.3 per cent deviations of more than  $\frac{1}{4}$  D distance led to the conclusion that each of these deviations could be attributed either to no change in the prescription after a certain lapse of time or to considerable changes in the addition for near vision. The smaller deviations of less than  $\frac{1}{4}$  D distance from the continuous curve (1) are caused by the lack of intervals finer than  $\frac{1}{8}$  D in the lenses of the trial case, which are graded in  $\frac{1}{8}$  D steps for the spheres and cylinders.

6 In the cases in which the two eyes differed during the period of observation by a constant sphere, it was more convenient to use instead of equation 1, a formula with four constants, one of which expresses this constant difference. This formula is

$$(3) \quad y = a' + A' (1 - 2^{-(x-s_0)/c})$$

where  $a'$ , the prepresbyopic value of  $y$  at the age  $s_0$ , may differ in the two eyes.  $a'$ ,  $s_0$  and  $c$  are identical for the two eyes.

The values of  $y$  calculated from formulas 1 and 3 do not differ for values of  $x$  greater than  $s_0$ .

For 60 cases the development of the addition for near vision could be studied together with the development of  $y$ , and both could be interpolated by the formula 1 and graphically represented by straight lines in the logarithmic diagram. The angle  $\alpha$ , the cotangent of which is  $c$  of formula 1, differed in the same case on the average only  $0.008^\circ$ , so that in these cases the trend in  $y$

and the trend in the decline of the power of accommodation proved to be essentially the same

7 The 80 cases of presbyopia of longest duration and maximum number of observations were used for prediction of the total refraction at the age of 65 from the knowledge of 4 or 5 prescriptions between the ages 40 and 50 years. At the age of 65, there was an average difference of 0.089 D between the predicted and the observed value of  $y$ .

8 It is concluded that the explanation of the exponential law requires (a) the adoption of the theory of senile hypermetropia, proposed by Her-

renheiser, which, to the exclusion of the postulation of tectonic changes, explains senile hypermetropia as the manifestation of preexisting hypermetropia temporarily compensated by a contraction of the ciliary muscle, and (b) a change in the theory of accommodation proposed by Helmholtz with regard to the dynamic aspect of the theory namely, that the decrease of accommodation with age is due to the increased resistance to the action of the ciliary muscle caused by the aging of the tissues of the zonula and the sclera.

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# ACCOMMODATION OF PRESBYOPIA AND ITS CORRECTION

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The correct addition for near vision in presbyopia depends primarily on the amount of available accommodation and secondarily on the selection of the best fixed distance for the near work

In correcting presbyopia, it has been customary among ophthalmologists to give the patient only one test, that is to determine the addition with which the patient "reads best" or feels most comfortable at the desired distance on the Prince rule. In ophthalmology one has at least three common methods of determining the correct distance refraction, or punctum remotum: (1) retinoscopic examination with cycloplegia, (2) trial case determinations with cycloplegia and (3) the postcycloplegia test. I recommend three methods for measuring the near point refraction, punctum proximum, or accommodation. I believe that the near point in the refraction of presbyopia is as important as the far point. Each of my three tests depends on distinctly different types of thresholds of visual sensation. There is no doubt of the statistical value of the measuring of samples in groups of three.

## RESERVE ACCOMMODATION

The reserve accommodation in presbyopia is that part of the total accommodation which must be set aside for comfort in doing ordinary continuous close work. For example, a patient with total accommodation of 1.50 D with an addition of a 2.00 D lens reads best at 40 cm (2.50 D on Prince's rule). The extra 1.00 D is the reserve accommodation. In this paper, I use a basic reading distance of 40 cm (2.50 D) as a standard in all my calculations. I shall show that exactly 1.00 D is the normal reserve accommodation which must be used in all presbyopic corrections. Hence, the total accommodation less +1.00 D is the available accommodation. By subtracting the patient's total accommodation from 3.50 D, one obtains the indicated addition for this basic distance of 40 cm.

## THREE METHODS OF MEASURING TOTAL ACCOMMODATION IN PRESBYOPIA

TEST 1 *The Near Blur Test*—With the patient's distance correction in place, determine his

total accommodation by Duane's method<sup>1</sup> or with my one-two line test.<sup>2</sup>

The one-two line test is as follows. With the distance correction before the right eye and with the left eye occluded, place a +1 to a +3 D spherical lens so that the near point will be about 25 cm from the eye. On one side and at the end of a small white card, place a fine black line, similar to Duane's black line on a white card. On the other side or opposite end of this card, place two similar parallel black lines, separated by an interval equal to the width of either line (figure, A). Present the parallel lines before the right eye much too close to be seen distinctly. Move these two parallel lines away from the eye until the patient sees two lines. Note the reading on the Prince rule. Then, bring the single line in until the patient announces that it is "slightly blurred," "worse" or "not so good." Repeat this process until the difference of the two readings is 2 cm or less. If there is still doubt as to the correct measurement of accommodation, place the fine print (figure, B) close to the patient's eyes. Tell him to read it aloud as soon as he can. Note the point on the rule where he begins to read. In measuring the accommodation, always record the blurring of the line coming in as diopters on the Prince rule and not as centimeters. There is a distinct advantage in thinking of the amounts of accommodation in terms of "diopters required" distance rather than of linear measurement.

TEST 2 *The "Reads Best" Test*—Place the indicated addition in front of the patient's distance correction and ask him where he "reads best" the fine print on the test chart. It is convenient to have this chart rectangular and mounted on a handle (figure, B). This should be read at 40 cm if the measurement of accommodation is correct. Hence, to test his accommodation in this manner, ask him where he reads this fine print best on the Prince rule with the indicated addition in the trial frame. This point

1 Duane, A. A Standard Test-Object for Determining the Near Point and Range of Accommodation, *Ophth Rec* 18:358-360 (July) 1909.

2 Slataper, F. J. Total and Reserve Accommodation in Presbyopia, *Texas State J Med* 21:536-540 (Jan) 1926.

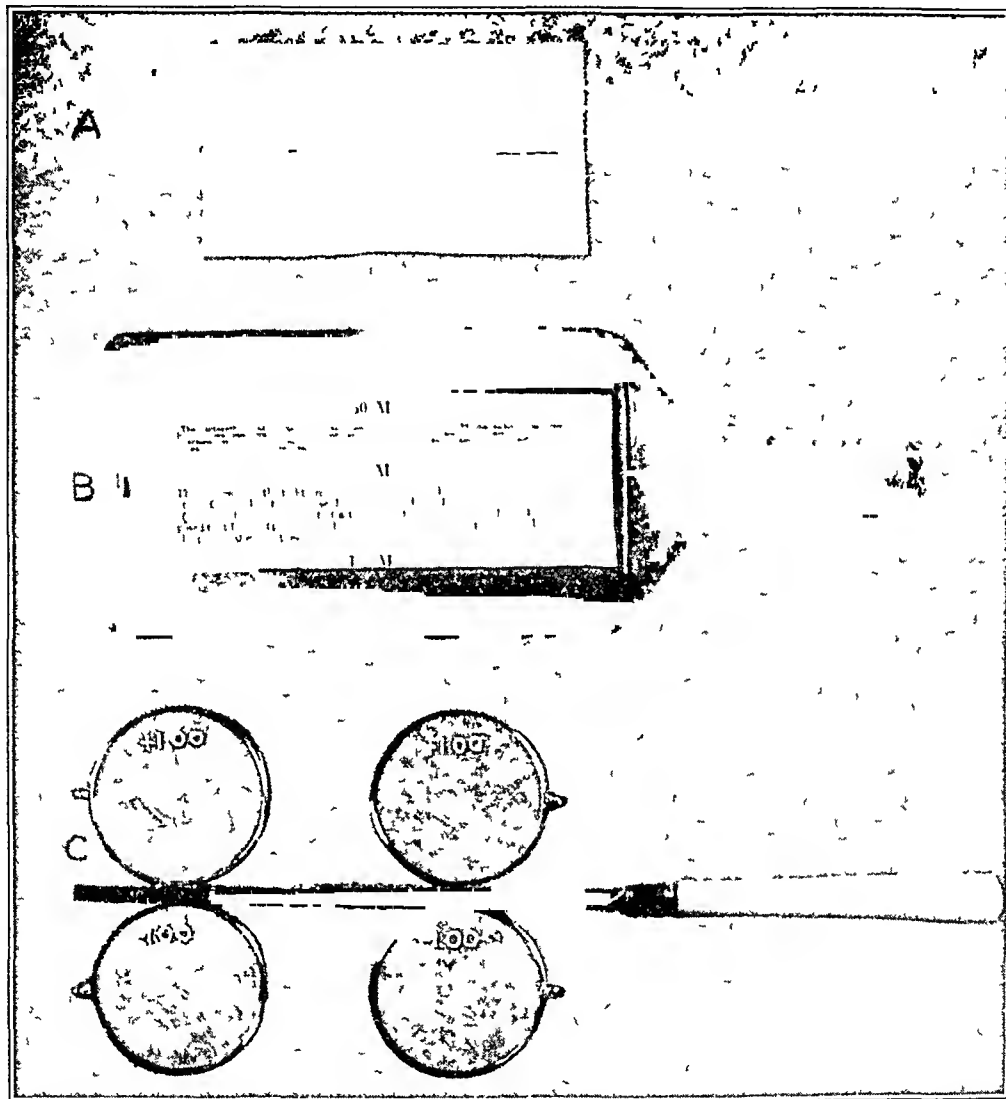


expressed as diopters minus the addition plus 1 00 D is his total accommodation

**TEST 3 The + and — 1 00 D Spheres Readability Test**—Now with +1 00 D spheres (figure, C) added to the correction for distance previously determined and the indicated addition, place the reading chart beyond 50 cm, slowly bring the chart toward the patient's eye and ask him to tell where he can read some of the letters of a word. I use a small, paddle-shaped frame to

spheres addition in two ways (1) Bring the print in from 50 cm until it is "partly readable," or (2) push the print out from about 25 cm until it is slightly blurred. Deduct 1 00 D to get the actual far point accommodation

Place a — 1 00 D sphere binocularly before each eye in place of the + 1 00 D spheres, as in the preceding test, and hold the chart close to the patient's eyes. Ask him to tell when he can read a few letters of a word of the fine print,



A, accommodation card, B, reading chart in handle, and C, + and — 1 00 D spheres on handle

hold the reading chart. This device enables the patient to place the small reading matter directly over the markings on the Prince rule. This chart becomes partly readable at or near 40 cm if the accommodation and the addition are correct. Record this "working far blur" accommodation in diopters. This "readability" or "blur" accommodation less 1 00 D is the patient's actual "far partly readable," or "far blur" accommodation.

The "far readability" or "far blur" accommodation can be determined with the + 1 00 D

which should become partly readable at 40 cm (2 50 D). This reading plus 1 00 D is his actual "near partly readable" or "near blur" accommodation, expressed in diopters. The "near readability" or "near blur" accommodation with — 1 00 D spheres can be measured in two ways: (1) Push the print out from about 25 cm until it becomes "partly readable," or (2) bring the print in from 50 cm until it becomes "slightly blurred." The average near and far blur readings should be at 40 cm (2 50 D), if the accommodation and addition are correct.

In this third test of the total accommodation, the "partly readable" procedure is more dependable than the "slightly blurred" determination because the ophthalmologist can check the patient's cooperation by hearing him read the words aloud. The "average near and far readability" accommodation less the addition plus 1.00 D is equal to his total accommodation. In case the patient has less than 5/5 vision, he should be examined for his "reads best" and his "average readability" accommodation at his "optimum" reading distance and not at 40 cm, e.g., a patient with a vision of 5/10 should be tested at 33 cm (table 5). The average "near and far readability" test with + and - 1.00 D spheres is the most accurate test of accommodation in cases of presbyopia.

*Comment*—The "reads best" test and the + and - 1.00 D spheres readability test can be used only in cases of presbyopia (3.50 D or less of accommodation). However, the one-two line test can be used for measuring any amount of accommodation if the patient has sufficient intelligence.

### TESTS OF COOPERATION

In making the preceding tests for the near point, if the results seem contradictory, the patient should be tested for his cooperation. There are three methods which I use for doing this.

1 *The Near Blur Cooperation Test*—Add or subtract a 1.00 D sphere from the addition in the trial frame. If his near blur accommodation does not change 1.00 D on the rule, he is not cooperating.

2 *"Reads Best" Cooperation Test*—Use a pair each of + and - 0.50 D spheres on a handle. Add + 0.50 D spheres to the addition for the near point and the correction for distance. His "reads best" accommodation should be 0.50 D nearer on the Prince rule than before. Now, reverse the procedure. Add - 0.50 spheres to the correction. The "reads best" accommodation will be 0.50 D less on the rule. This test is a quick method of proving the patient's cooperation. If the patient fails to change the point on the Prince rule by 0.50 D, he is not cooperating.

3 *The + and - 1.00 D Spheres "Partly Readable" Average Cooperation Test*—Change the addition in the trial frame 0.50 or 1.00 D. Then find the average "far partly readable" accommodation with + and - 1.00 D spheres. The average should be exactly the amount by which the addition in the trial frame was changed.

*Comment*—When one finds a patient who does not cooperate in one of the aforementioned tests,

ignore that test and use the other two. Do not allow the patient to know that he is not cooperating. Tell him that the patient is always right and that all of the mistakes are yours. Many of the patients who say they are ten years younger than their real age are also guilty of not cooperating in one of these cooperation tests. I have never seen a patient who could fool me in more than one of the tests because each of the three methods depends on a different type of threshold of visual sensation.

### HISTORY OF THE THREE ACCOMMODATION TESTS

Soon after I began the private practice of ophthalmology, I became convinced that the correct addition for presbyopia should be based on the patient's accommodation and not on his alleged age. From the beginning, I have measured the accommodation in diopters by a near blur test (Duane's method or my one-two line test) in all cases of refraction except those of young children and aphakic persons. After three years of practice, I stated:

The amount of sphere added for near in an ordinary case of presbyopia depends upon three factors: the working distance, the total accommodation, and the reserve accommodation.<sup>3</sup>

In that study of normal reserve accommodation,<sup>3</sup> I made some mistakes, which were due to wrong "assumptions." One such assumption was that the average working distance of all presbyopic corrections was 33 cm, instead of 40 cm, which is more nearly correct. Again, the assumption of an "average addition of 3.00 D for a patient of 60 years with normal vision" was not correct. In that paper, the reserve for 2.50 D accommodation or less varied from 1.21 to 1.00 D instead of being exactly 1.00 D.

When, in September 1935, I began the individual tests of the first series (200 cases), I was ignorant of the relation of the average blur test to the "reads best" and the "near blur" accommodation test. In that series, I found that the "average near and far blur" test was a practical test for accommodation.

In the second series of tests (100 cases), begun in January 1940, I made the following observation: 1. With the aid of the + and - 1.00 D spheres, the "average near and far blur" accommodation could be measured better at 40 cm. than without them at 66 and 28 cm. This eliminated the confusion of the patient between sharpness of focus and magnification and minification.

3 Slataper, F. J. The Normal Reserve Accommodation in Presbyopia, *Arch. Ophth.* 55:370-376 (July) 1926.

of the test object 2 The "blur amplitude" was 2 00 D Having become aware of these two facts, I began the third series of tests

About November 1941, I began the routine of taking the average near and far blur readings with the + and - 1 00 D spheres in the fitting of glasses for presbyopia as a check on the "reads best" and the "indicated addition" determination based on the near blur (Duane's or my one-two line) test for the total accommodation In the individual cases of the third series (300 cases) the measurements of average readability or average blur accommodation were all taken with the + and - 1 00 D spheres to prevent the confusion of the test objects by their being magnified or minified

### THEORETIC CONSIDERATIONS

The presbyopic eye corrected for distance and for near vision in getting a sharp retinal picture is similar to a camera being focused for a close-up photograph and follows some of the same laws of optics

#### DEFINITIONS

The point on a Prince rule at which the patient "reads best" corresponds to the best focus of the camera

In the eye, the "near blur" point on the rule represents the nearest area of the picture sufficiently in focus to be partly recognizable

In the eye, the "far blur" point represents the part of the picture farthest from the anterior focus of the eye where print is partly recognizable The near and the far blur point are always measured in diopters from the eye

In the eye, the area between the near and the far blur point is called the blur amplitude

In the camera, the area between these two points is called the depth of focus

The near blur point is obtained by bringing fine print or a line in toward the eye until it blurs or by pushing print or two lines out away from the eye until it is partly readable

The far blur point is obtained by pushing print out until it blurs or by bringing it in from a distance until it is partly readable

The near and far blur points are practically the same, respectively, as the near and far "partly readable" points The slight difference of measurements by these methods is that of the reaction times of the patient and of the ophthalmologist This is always made less with practice

#### DEDUCTIONS

1 *Algebraic Demonstration of Blur Amplitude*—In the corrected presbyopic eye, as in a

camera, the sum of the near and far blur points divided by 2 is always equal to the "reads best" point or "best focus" when measured in diopters from the anterior focus of the eye, as demonstrated by the following formula

A well known formula<sup>4</sup> for measuring depth of focus as distance in photography is as follows

$$\frac{F B \text{ distance} \times N B \text{ distance}}{F B \text{ distance} + N B \text{ distance}} \left\} \times 2 = \text{best focus, or } Y$$

To convert distance in meters into diopters, divide unity by the distance Substituting diopters for distance in this formula

$$\frac{\frac{1}{F B} \times \frac{1}{N B} \times 2}{\frac{1}{F B} + \frac{1}{N B}} = \frac{1}{Y} \quad \frac{\frac{2}{F B \times N B}}{\frac{N B + F B}{F B \times N B}} = \frac{1}{Y}$$

Inverting the terms of the divisor and multiplying

$$\frac{2}{F B \times N B} \times \frac{N B \times F B}{F B + N B} = \frac{2}{F B + N B} = \frac{1}{Y}$$

$$\frac{2}{F B + N B} = \frac{2}{2Y}$$

In equal fractions, if the numerators are equal, the denominators are equal

Therefore  $F B + N B = 2 Y$

$$\text{or } \frac{F B + N B}{2} = Y$$

expressed as diopters

Therefore, the average blur point equals the best focus in terms of diopters Hence, as in photography, the average of the near and the far blur point, when expressed as diopters, is equal to the best focus That is, the "reads best" point is equal to the "average near and far blur" point in a presbyopic correction for near vision

2 *Normal Reserve Accommodation*—In my three series of cases, I proved that the normal reserve accommodation of presbyopia is exactly 1 00 D This means that the near blur accommodation is 1 00 D less than the "reads best" accommodation, since

$$\frac{F B + N B}{2} = Y$$

as proved, or  $N B + F B = 2 Y$

4 Stubbs, S G B ' The Modern Encyclopedia of Photography, Boston, American Photographic Publishing Company, 1940, vol 1, p 523

Since the near blur accommodation is the normal reserve accommodation and always is equal to 1.00 D, by substituting  $Y - 1$  for  $N B$

$$\begin{aligned} F B + Y - 1 &= 2 Y \\ F B &= Y + 1 \end{aligned}$$

Now, since  $F B = Y + 1$  and  $N B = Y - 1$ , the difference in the value for  $N B$  and that for  $F B$  is 2.00 D

Hence, the far blur accommodation is equal to the "reads best" accommodation plus 1.00 D. Therefore, the depth of focus, or blur amplitude, in presbyopia is 2.00 D, and the near blur is always equal to the far blur

**3 Physiologic Demonstration of Blur Amplitude**—This principle that "the average blur" accommodation is always equal to the "reads best" accommodation can be demonstrated with a patient under a cycloplegic after the examiner has finished his refraction at 5 meters. Add +2.50 D spheres to his correction for distance. He will read with this best at 36 cm (2.75 D). His far blur accommodation will be 2.75 D, with +1.00 D added to his correction, and his near blur accommodation, 2.75 D, with -1.00 D spheres added in place of the +1.00 D spheres. Subtracting and adding 1.00 D gives his far blur point at 1.75 D and his near blur point at 3.75 D, that is, 1.75 D plus 3.75 D divided by 2 equals 2.75 D. He reads with a +2.50 D addition best at 36 cm (2.75 D) because his distance refraction was determined at 5 meters (0.20 D) instead of at infinity.

In two series of patients, 10 presbyopes and 10 nonpresbyopes given refraction under homatropine cycloplegia, this observation of a difference of 2.00 D was confirmed for each of the 20 patients. Patients under atropine cycloplegia were given similar tests, with the same results.

This blur amplitude (near blur minus far blur reading) is always 2.00 D, as proved physiologically in the preceding paragraph and by the laws of optics shown in section 2.

**4 Analysis of Blur Amplitude**—This 2.00 D of blur amplitude consists of two parts: (1) the true depth of focus, 0.58 D, and (2) the nonparalyzable accommodation of 1.42 D. Ogle<sup>5</sup> has shown that the human eye has an average depth of focus of 0.5 to 0.66 + D (average 0.58 D). "The mean of all in table 2 was 0.566."<sup>5</sup>

What is responsible for this 1.42 D power of accommodation found during cycloplegia and in the presbyope wearing a correction for near vision? It must be due to changes in the posi-

tion or shape of the lens, because in cases of aphakia I find that the blur amplitude varies from 0.5 to 0.66 + D, in agreement with Dr. Ogle, and not 2.00 D. It cannot be due to the intraocular ciliary muscles, which are not paralyzed by a cycloplegic, because in any presbyope exactly the same blur amplitude of 2.00 D occurs without cycloplegia as with complete cycloplegia. Could it be due to the extraocular muscles pressing on the vitreous, causing lenticonus, or to a displacement of the lens along the axis of the eye about 0.568 mm backward for the far blur accommodation and 0.568 mm forward for the near blur accommodation? According to the lenticonus-vitreous pressure theory a negative pressure would be required for the far blur accommodation. This is impossible on account of the collapsible walls of the sclera. The displacement theory appears the more plausible, that is, the shifting of the lens backward or forward, as in the fishes, of about 0.568 mm in each direction accounts for 1.42 D of accommodation.

The mechanism of accommodation consists of two types: (a) Change in the shape of the lens. This is abolished by a cycloplegic and ceases with advanced presbyopia. (b) Shifting of the lens forward or backward. This causes most of the 1.00 D change for near or far vision, which is not affected by cycloplegia or presbyopia and must be used as the normal reserve in the fitting of presbyopia corrections for near vision. Reading at the near blur point for long periods quickly becomes tiresome. Reading at the far blur point causes the eyes to have the sensation of "drawing" and may become painful.

**5 Changes in the Visual Angle**—Many patients confuse sharpness of focus with magnification. The height or tangent of the tall letters of Thorington's +0.50 D type on a reading test card is about 2 mm, or 17 minutes of angle at 40 cm. When viewed for comparison, a letter of the same height shows an experimental visual angle of 10 minutes at 66.6 cm and of 24 minutes at 28.5 cm. These are the distances of the presbyope's far and near blur accommodation when fitted with a glass for near work at 40 cm.

In measurement of the blur accommodation at the far point 66.66 cm, and at the near point, 28.57 cm, the same letters occupy 2.4 times as large a visual angle at the near blur as at the far blur point. This type of magnification, a larger retinal picture, makes the test object appear more readable while the actual focus may not be so good. If the near and the far blur accommodation are tested each at 40 cm, this confusion of magnification, minification and sharp-

<sup>5</sup> Ogle, K. N. Measurements on the Depth of Focus of the Human Eye, with Various Test Objects, Masters Thesis, Dartmouth College, Hanover, N. H., 1927.

ness of focus can be eliminated. Since the blur amplitude was exactly 2.00 D, an addition of +1.00 D for the far blur and a -1.00 D for the near blur accommodation would be ideal. Hence, to test these blur or readability accommodations at 40 cm, add to the selected presbyopic correction -1.00 D spheres for the near and +1.00 D spheres for the far point. I used a pair of + and a pair of -1.00 spheres on a handle for this purpose (figure, C). The increased accuracy in these tests for near and far blur accommodation in my third series of cases was ample proof of the usefulness of the method.

**6 Accommodation Formulas**—Since the normal reserve accommodation in correcting presbyopia is 1.00 D, 3.50 D less the total accommodation is the standard addition for reading at 40 cm.

My formulas for total accommodation threshold tests are as follows:

1 The near blur test (my one-two line test or Duane's test). The near blur accommodation less the addition equals the total accommodation.

2 The "reads best" test. The "reads best" accommodation less the addition +1.00 D equals the total accommodation.

3 The + and -1.00 D spheres test (average readability or blur test). The average readability or blur accommodation less the addition plus 1.00 D equals the total accommodation.

4 Far blur or far readability test. The far blur or the far readability accommodation less the addition plus 2.00 D equals the total accommodation.

Duane's test is the one most often described by writers on accommodation. The "reads best" principle is most often used in prescribing lenses for near vision, but it is not recognized as an actual test of total accommodation. However, in presbyopia, it is the second most accurate single method of measuring total accommodation. The average blur test with the + and -1.00 D spheres is the most accurate accommodation test because it depends on two separate thresholds of sensation, which are easily compared at the same distance. This observation was confirmed by results in my third series of cases. The far blur test is the least accurate single test because it is more difficult for the patient to comprehend and cooperate.

In my hands, the near blur method is always used as a monocular test, the "reads best" and the + and -1.00 D spheres (average readability or blur) method are always binocular tests in the determination of a presbyotic correction. I always make the three tests in the order indicated.

## NORMAL RESERVE ACCOMMODATION

The average total accommodation in each case was determined by taking a third of the sum of total accommodation obtained by the three methods: (1) my one-two line procedure, (2) the "reads best" method and (3) the + and -1.00 D spheres average blur test.

$$\text{Average total accommodation} = \frac{1-2 \text{ line acc} + \text{"reads best" acc} + \text{avg blur acc}}{3}$$

The reserve accommodation in each of the 600 cases was figured from the average accommodation. This average accommodation was figured by two methods in the first series, of 200 cases, and by three methods in the second series, of 100 cases, and in the third series, of 300 cases. The reserve was figured according to the following formula: Average accommodation plus the addition minus 2.50 D, the standard distance accommodation, equals the normal reserve accommodation.

$$\text{Average accommodation} + \text{addition} - 2.50 \text{ D} = \text{normal reserve accommodation}$$

## STATISTICS ON NORMAL RESERVE ACCOMMODATION (Tables 1 and 2)

In table 1, the normal reserve accommodation for the additions of 1.00 to 2.50 D, inclusive, are shown as averages in 600 cases. As my work became more accurate in the succeeding series, the normal reserve accommodation approached closer to 1.00 D. The mean deviation, the standard deviation and the probable error consistently became less. This is shown in table 2. Thus, in the last series one could say that the normal reserve accommodation is exactly 1.00 D.

In a similar manner, I made a small series of tests with additions from 2.75 to 3.50 D and found the normal reserve accommodation to be exactly 1.00 D.

## RELATIVE ACCURACY OF THE THREE ACCOMMODATION TESTS (Tables 3 and 4)

In the third series, of 300 cases, the one-two line accommodation test was found to be the most frequently wrong. It showed an error of 16.33 + per cent. The "reads best" accommodation test was wrong in 2.33 + per cent of the cases. The + and -1.00 D spheres readability accommodation test was the most accurate, as it showed an error of 0.33 + per cent.

The fact that the tests are always made in the order indicated tends to make the last test the most accurate. However, this factor will not account for the great difference in their accuracy.

A glance at table 4, presenting a summary of the average values for the three accommodation tests, will show the relative accuracy in this series. For the "reads best" and the + and - 1.00 D spheres average blur accommodation test the mean deviation, the standard deviation and the probable error are much less in the third series than in the first and second series. The more I worked with accommodation, the less reliable I found the near blur test (my one-two line test and Duane's test)

TABLE 1—Statistics on Normal Reserve Accommodation

Addition, D	Normal Reserve Accom- modation	Mean Deviation	Standard Deviation	P. E.
First Series (200 Cases)				
1.00	0.98	0.05	0.52	0.351
1.25	1.02	0.07	0.75	0.500
1.50	0.98	0.04	0.46	0.310
1.75	0.99	0.05	0.61	0.411
2.00	0.99	0.05	0.65	0.438
2.25	1.00	0.04	0.57	0.384
2.50	1.02	0.04	0.46	0.310
Total	0.98	0.04	0.02	2.710
Average	0.997	0.048	0.574	0.387
Second Series (100 Cases)				
1.00	0.992	0.035	0.051	0.034
1.25	0.981	0.052	0.080	0.054
1.50	1.008	0.031	0.075	0.030
1.75	0.965	0.042	0.046	0.031
2.00	1.002	0.023	0.042	0.028
2.25	0.994	0.025	0.044	0.030
2.50	1.025	0.032	0.035	0.024
Total	0.967	0.040	0.373	0.231
Average	0.995	0.034	0.053	0.033
Third Series (300 Cases)				
1.00	1.000	0.008	0.023	0.0157
1.25	1.002	0.007	0.010	0.0110
1.50	1.002	0.003	0.007	0.0052
1.75	0.994	0.009	0.015	0.0102
2.00	1.001	0.002	0.006	0.0043
2.25	1.002	0.021	0.002	0.0013
2.50	1.010	0.009	0.024	0.0168
Total	7.011	0.059	0.093	0.0645
Average	1.001	0.008	0.013	0.0092

TABLE 2—Summary of Data in Table 1

Series	Average Reserve Accom- modation	Mean Deviation	Standard Deviation	Probable Error
First	0.997	0.048	0.574	0.387
Second	0.995	0.034	0.053	0.033
Third	1.001	0.008	0.013	0.0092

## BEST FIXED DISTANCE

After the patient's total accommodation is decided on, the next step is to determine his proper reading distance.

The best fixed distance for near work depends on the following factors

*Visual Acuity*—The best reading distance is most easily determined by the visual acuity, as

shown by table 5. This table is based on visual efficiency, as shown by Snell<sup>6</sup> and Snell and Sterling<sup>7</sup> and used by Lebensohn<sup>8</sup> in his "near vision test charts." It is assumed that 40 cm is the average normal reading distance for 20/20 vision. Hence, the best reading distance for any visual acuity is obtained by multiplying the visual efficiency of that acuity by 40 cm.

With a visual acuity of 20/200 or 20/100, reading is impossible except for short periods of time. A + 13.00 D lens held in the hand is a more practical glass for near vision than when it is placed in a spectacle. A + 4.00 D addition is about as strong an addition in a bifocal as can be used. This often forms a very useful glass for a patient with vision of 20/70. A patient with 20/40 vision should never be fitted for any distance beyond 33 cm from his eye. I know several presbyopic bookkeepers with this vision who are very efficient in their work.

If the patient has unequal vision, the average "diopters required" distance of each eye should be used, provided that the difference is 1.00 D or less (table 5). If the difference is more than 1.00 D, then the patient should be fitted as for "monocular vision" in the better eye. The following examples may be given.

Vision of 20/60 in the right eye requiring 3.50 D and vision of 20/20 in the left eye requiring 2.50 D gives a difference of 1.00 D. The sum of 2.50 D and 3.50 D divided by 2 equals 3.00 D, the average diopters of correction required. The patient should be fitted for 33 cm.

Again, vision of 20/70 in the right eye requiring 4.00 D and vision of 20/16 in the left eye requiring 2.25 D gives a difference of 1.75 D. The patient should be fitted as for monocular vision. Now, 2.25 D plus 0.25 D equals 2.50 D, at a distance of 40 cm. Bifocals of the same strength as the glass for the better eye are optional.

The patient should not be given unequal additions for unequal vision, because each eye requires the same amount of normal reserve accommodation. Unequal additions should be given only for unequal total accommodation, which is rare.

6 Snell, A. C. Visual Efficiency of Various Degrees of Subnormal Visual Acuity, *J. A. M. A.* 85: 1367-1373 (Oct. 31) 1925.

7 Snell, A. C., and Sterling, S. Percentage Evaluation of Macular Vision, *Arch. Ophth.* 54: 443-461 (Sept.) 1925.

8 Lebensohn, J. E. Scientific and Practical Considerations Involved in the Near-Vision Test with Presentation of a Practical and Informative Near-Vision Chart, *Am. J. Ophth.* 19: 110-117 (Feb.) 1936.



*Muscular Balance*—With poor convergence, the patient should be fitted for as far a point as is consistent with reading efficiency. A patient with an excessive convergence should be fitted from 0.25 to 0.50 D closer than a patient with normal muscle balance. If he has no fusion at the near point, he should be fitted for monocular vision. Bifocals of unequal additions may be

should be fitted for 57 or 60 cm. Both these occupations require extra high, large bifocals. The linotype operator needs the bifocals of the same shape.

In many occupations the bifocal segment must be very low and very small, as in the case of a railroad conductor, truck driver, head janitor or rifleman.

TABLE 3—Summary of Data on the Three Accommodation Tests

Addition, D	Average Accom- moda- tion	"1 2 Line" Accommodation				"Reads Best" Accommodation				Average Blur Accommodation			
		Total Accom- moda- tion	Mean Devia- tion	Stand- ard Devia- tion	P E	Total Accom- moda- tion	Mean Devia- tion	Stand- ard Devia- tion	P E	Total Accom- moda- tion	Mean Devia- tion	Stand- ard Devia- tion	P E
First Series (200 Cases)													
1 00	2 48	2 49	0 07	0 12	0 081	2 51	0 08	0 097	0 065	2 45	0 08	0 11	0 074
1 25	2 27	2 30	0 17	0 18	0 121	2 28	0 08	0 098	0 066	2 24	0 10	0 13	0 088
1 50	1 98	1 98	0 05	0 071	0 048	2 00	0 06	0 098	0 067	1 96	0 08	0 098	0 067
1 75	1 74	1 74	0 07	0 087	0 039	1 76	0 05	0 065	0 044	1 74	0 08	0 10	0 067
2 00	1 49	1 49	0 05	0 069	0 046	1 52	0 06	0 084	0 057	1 49	0 07	0 087	0 039
2 25	1 25	1 23	0 06	0 084	0 057	1 29	0 072	0 09	0 061	1 21	0 01	0 12	0 031
2 50	1 02	1 00	0 039	0 046	0 031	1 03	0 053	0 083	0 056	1 02	0 069	0 11	0 074
Total			0 509	0 657	0 443		0 455	0 615	0 416		0 509	0 755	0 510
Average			0 072	0 093	0 063		0 065	0 088	0 059		0 072	0 107	0 072
Second Series (100 Cases)													
1 00	2 49	2 48	0 05	0 09	0 061	2 50	0 03	0 052	0 035	2 50	0 02	0 042	0 025
1 25	2 23	2 25	0 06	0 11	0 074	2 24	0 02	0 044	0 030	2 20	0 05	0 10	0 067
1 50	2 01	2 00	0 05	0 084	0 057	2 00	0 03	0 046	0 031	2 00	0 03	0 046	0 031
1 75	1 71	1 62	0 11	0 17	0 115	1 77	0 05	0 077	0 052	1 75	0 07	0 098	0 066
2 00	1 50	1 51	0 04	0 082	0 055	1 50	0 02	0 041	0 028	1 50	0 02	0 038	0 026
2 25	1 24	1 19	0 06	0 12	0 081	1 26	0 04	0 086	0 058	1 28	0 04	0 096	0 065
2 50	1 02	1 02	0 03	0 058	0 037	1 06	0 06	0 10	0 067	0 96	0 09	0 19	0 128
Total			0 400	0 714	0 482		0 230	0 446	0 301		0 320	0 610	0 411
Average			0 057	0 102	0 069		0 035	0 063	0 043		0 045	0 087	0 059
Third Series (300 Cases)													
1 00	2 500	2 500	0 013	0 042	0 0283	2 508	0 013	0 040	0 0270	2 496	0 009	0 033	0 0222
1 25	2 250	2 338	0 091	0 143	0 0964	2 261	0 021	0 051	0 0344	2 240	0 010	0 024	0 0162
1 50	2 002	1 940	0 081	0 187	0 1261	2 005	0 003	0 018	0 0121	2 000	0 001	0 008	0 0034
1 75	1 744	1 716	0 091	0 177	0 1193	1 738	0 008	0 028	0 0191	1 746	0 005	0 014	0 0095
2 00	1 501	1 473	0 115	0 268	0 1809	1 504	0 003	0 014	0 0095	1 500	0 001	0 006	0 0047
2 25	1 252	1 246	0 049	0 118	0 0795	1 258	0 006	0 030	0 0202	1 250	0 003	0 014	0 0094
2 50	1 011	1 010	0 018	0 050	0 0337	1 024	0 016	0 045	0 0303	1 006	0 009	0 024	0 0162
Total			0 458	0 985	0 6642		0 070	0 226	0 1526		0 038	0 123	0 0831
Average			0 065	0 147	0 0949		0 010	0 032	0 0218		0 005	0 017	0 0119

TABLE 4—Summary of the Averages of the Three Accommodation Tests (Table 3)

Series	"1 2 Line" Accommodation			"Reads Best" Accommodation			Average Blur Accommodation		
	Mean Devia- tion	Standard Devia- tion	P E	Mean Devia- tion	Standard Devia- tion	P E	Mean Devia- tion	Standard Devia- tion	P E
First	0.072	0.093	0.063	0.065	0.088	0.039	0.072	0.107	0.072
Second	0.057	0.102	0.069	0.035	0.063	0.043	0.045	0.087	0.059
Third	0.065	0.147	0.0949	0.010	0.032	0.0218	0.005	0.017	0.0119

found convenient in some cases of external and internal strabismus with fair vision in each eye.

*Nature of Occupation*—Many occupations require a special glass for the office, to be used only at work. The patient has an extra pair of general utility glasses which he uses most of the time. As examples: The stenographer with 20/16 vision using a Line-a-time copy holder most of the day should be fitted for 50 cm. The pianist

TABLE 5—Optimum Presbyopic Reading Distances Based on Visual Acuity

Acuity		Diopters Required	Distance, Cm	Visual Efficiency, %
5/61	20/200	12.50	8.0	20
5/30	20/100	5.00	19.6	49.9
5/21	20/70	4.00	25.5	63.8
5/15	20/60	3.50	28.0	69.9
5/12	20/50	3.25	30.6	76.5
5/10	20/40	3.00	33.4	83.6
5/7.5	20/30	2.75	36.6	91.4
5/6	20/25	2.62	38.2	95.6
5/5	20/20	2.50	40.0	100
5/4	20/16	2.25	44.0	110

*Length of Arms*—The person with long arms may be fitted differently from the person with very short arms

*Monocular Vision*—A person with monocular vision should have an addition of  $+0.25$  D more than the rule

Duane<sup>9</sup> has shown that in cases of presbyopia the binocular accommodation on an average is  $0.25$  D greater than the monocular accommodation. He suggested "We must reckon with this fact in giving him a reading glass, which must, as a rule, be at least  $0.50$  D stronger than if he were two-eyed"

*Old Reading Habits*—Many myopes with high astigmatism have acquired the habit of reading 30 to 36 cm from their eye by taking off their glasses. These patients may be fitted with their bifocals to read at this distance to keep them happy. The same principle applies to a patient who has long worn an overcorrection for near work.

Many presbyopes have never worn a correction for near work until they need a very strong addition. These patients are more comfortable if they are fitted for 44 cm rather than 40 cm

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<sup>9</sup> Duane, A. Monocular and Binocular Accommodation, *Tr Am Ophth Soc* **20** 132-157, 1922

## CONCLUSIONS

1 The correct estimation of the patient's total accommodation is the most important factor in the correction of presbyopia with a glass for near work

2 It is necessary to use three types of tests to measure accurately the total accommodation in many patients

(a) The near blur test—after Duane

(b) The "reads best" test—the most common method

(c) The  $+$  and  $-1.00$  D spheres average readability test

One must continue with these three tests in the order indicated until the readings are all made at the same point on the Prince rule. This procedure seldom fails

(d) The  $+$  and  $-0.50$  D spheres cooperation test will show the cause in case of failure

3 The normal reserve accommodation for all near work is exactly  $1.00$  D

4 The available accommodation for near work is the total accommodation less  $1.00$  D

5 The best fixed distance for close work depends on the following factors (a) visual acuity, (b) nature of occupation, (c) muscle balance, (d) length of arms, (e) monocular or binocular vision and (f) long-established reading habits

1110-1111 Medical Arts Building

# REMOVAL OF THE DISLOCATED LENS UNDER A CONJUNCTIVAL POCKET FLAP

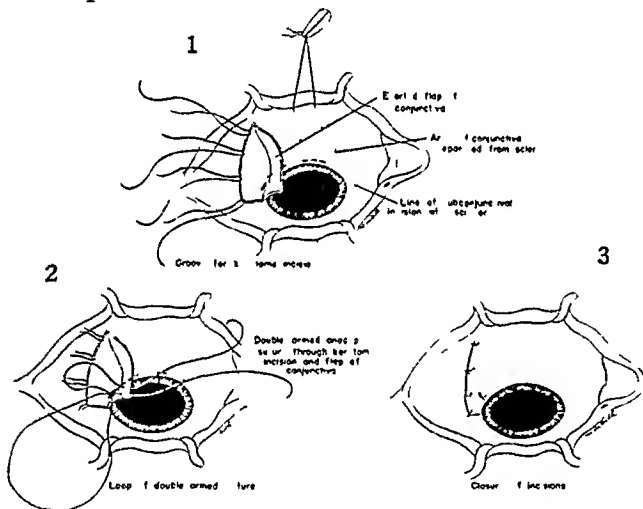
ROBERT STEELE IRVINE, M D  
SAN FRANCISCO

Utilizing ideas from several operators and adding some of my own, I have developed and used in 10 cases a technic emphasizing the following features

1 A vertical incision of the conjunctiva, about 13 mm long, beginning 5 mm from the limbus, at 9 o'clock in the left eye and at 3 o'clock in the right eye

2 Wide separation of the conjunctiva over the upper half of the globe

3 Opening of the anterior chamber, with a keratome incision, under the everted edge of the flap



Steps in the formation of a conjunctival pocket flap for removal of the dislocated lens

4 Completion of the section, with scissors, under the flap

5 Extraction of the lens with the loop, depressing the sclera under the flap

6 A water-tight closure of the incision

Control of the eye is obtained with the usual akinesis, retrobulbar injection and superior rectus traction suture. The iris is widely dilated with a short-acting mydriatic. No iridectomy is done. Contraction is maintained for several days with physostigmine.

A groove is made under the everted lower edge of the flap with a Bard-Parker no. 15 blade at the 2 o'clock position in the left eye and the 10 o'clock position in the right eye, and a double-armed silk suture blade secured to an eyeless needle is placed through the cornea at half its

depth, the needles pointing in opposite directions. The loop is drawn out, with the threads held apart, and the keratome enters the bottom of the groove, between the two bites. These needles are afterward pulled through the overlying flap, and the suture is tied outside.

Four single-armed silk sutures are placed through the lateral lip of the conjunctival incision, including a small bite of the episclera, and are turned aside, prior to making the section. After extraction of the lens, these sutures are passed through the other edge of the flap and tied, completing the closure.

I have found the most difficult detail to be the placing of the suture through half the layers of the cornea and the correct placing of the keratome incision. I believe, however, that this step is of the utmost importance.

I have had the following complications:

1 Once the suture was caught and divided by the point of the keratome. The suture was re-applied, after the section, without difficulty.

2 Once the lens was drawn up, resulting in elevation of the pupil. This was relieved by iridotomy below.

There have been up to this time no retinal separations.

I have been surprised at the small loss of vitreous. My only explanation is that the positions of the conjunctival and corneal incisions do not coincide. I consider this flap considerably safer than the conjunctival bridge, and I present the method as a fairly safe procedure for the operator of average skill, with the expectation that the ingenious ones will improve on it.

Before submitting this article, I searched the literature for a description of a similar method, and the nearest I could find was one by Czermak<sup>1</sup> of a similar flap made below the equator and one by Tood (1915) of an undermining flap, formed with a knife incision. Neither of these procedures, in my opinion, has all the advantages of the method I have described.

490 Post Street

<sup>1</sup> Cited by Graefe, A., and Saemisch, T. *Handbuch der gesamten Augenheilkunde*, Leipzig, Wilhelm Engelmann, 1907, vol. 2.

# FOSTER KENNEDY SYNDROME WITH POST-TRAUMATIC ARACHNOIDITIS OF OPTIC CHIASM AND BASE OF FRONTAL LOBES

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PHILADELPHIA

The syndrome of atrophy of the optic nerve of one eye and papilledema in the other eye has come to be regarded as evidence of a tumor lying at the base of the frontal lobe. This relation was first pointed out by Paton<sup>1</sup> (1909) and was further elaborated on by Foster Kennedy<sup>2</sup> (1911). Recent studies have indicated that the syndrome may be found at times in association with arteriosclerosis of the internal carotid arteries, which compress the optic nerves and chiasm.<sup>3</sup> Recognition of this observation has tended to indicate that the Foster Kennedy syndrome is found at times in conjunction with disorders other than tumor and has led to elaboration of the conditions under which the syndrome may occur. Experience with a recent case indicates that it may develop also as a result of arachnoiditis in the region of the optic nerves and optic chiasm.

## REPORT OF A CASE

*History*—S S, a man aged 42, was admitted to the neurologic service of the Jefferson Medical College Hospital on Oct 24, 1944 with the complaints of blurred vision and occipital headache. Two weeks before admission he had been struck on the back of the head and rendered unconscious. He was taken to the accident ward of another hospital and discharged after observation, but he continued to complain of occipital headache and appeared mentally dull after the accident. He exhibited progressive mental torpidity and continued to complain of headache. For this reason he was admitted to the hospital for study.

*Examination*—Physical examination revealed good development. The patient showed a recent memory defect, in which retention and recall were impaired. Olfaction was preserved. The pupils were equal in size and shape, and both reacted well to light and in accommodation. Examination of the fundi revealed

pallor of the left optic disk with blurring of the nasal edge and 3+D of edema of the right optic disk. There were weakness of the right side of the face of central type, slight weakness of the right hand grip and pronounced unsteadiness in gait. The remainder of the neurologic examination revealed nothing significant.

Repeated examinations of the visual fields showed generalized constriction of the peripheral fields of vision, more advanced in the left eye. There was a central scotoma on the left side. The right blindspot was enlarged. Uncorrected visual acuity was 20/200 in the left eye and 20/30 in the right eye. Roentgenograms of the skull revealed the presence of a linear fracture in the right occipital bone extending from the region of the internal occipital protuberance through the floor of the right cerebellar fossa. The sella turcica was normal, as were the optic foramina. Lumbar puncture yielded clear, colorless spinal fluid under an initial pressure of 320 mm of water. The total protein content of the spinal fluid was 44 mg per hundred cubic centimeters. The Wassermann and Kahn reactions of the blood and of the spinal fluid were negative. The electroencephalographic tracings revealed no abnormality in either the resting record or during hyperventilation.

*Course*—On the basis of the neurologic and laboratory observations, it was felt that the patient had a brain tumor. Because of the Foster Kennedy syndrome, a basofrontal lesion (meningioma of the anterior fossa) seemed most probable. The absence of olfactory disturbances and the incoordination of gait were disturbing, and a ventriculographic examination seemed indicated. The ventriculograms showed that both lateral ventricles were tremendously dilated symmetrically, with no midline shift and that no air was visible in the third ventricle. The latter observation pointed to the possibility of a tumor in the anterior portion of the third ventricle. Combined encephalographic and ventriculographic examination was attempted but was unsuccessful.

Visual acuity became progressively decreased. About three weeks after his entrance into the hospital the uncorrected visual acuity was 20/200 in the right eye, while the left eye was blind. The Foster Kennedy syndrome persisted. In view of the rapid visual loss and the ventriculographic evidence of a tumor of the third ventricle, exploration was made on November 26, one month after the patient's entrance into the hospital and six weeks after the injury. A transfrontal craniotomy on the left side was performed. Over the entire dura covering the left frontal lobe was a thin hemorrhagic membrane, evidently the result of a hemorrhage of less than six months' duration. As the frontal lobe on that side was examined, it was found firmly attached at its anterior end to the dura by a band of adhesions roughly 1½ inches (3.8 cm) in length and ½ inch

From the Department of Neurology, Jefferson Medical College of Philadelphia.

1 Paton, L. A Clinical Study of Optic Neuritis in Its Relationship to Intracranial Tumors, Brain **32** 68, 1909.

2 Kennedy, F. Retrobulbar Neuritis as an Exact Diagnostic Sign of Certain Tumors and Abscesses in the Frontal Lobes, Am J M Sc **141** 355, 1911.

3 Yaskin, H E, and Schlezinger, N S. Foster Kennedy Syndrome Associated with Non-Neoplastic Intracranial Conditions, Arch Ophth **28** 704 (Oct) 1942.

(127 cm) in width. In fact, the dura appeared as though there had been an old underlying fracture at this point, which was approximately above the left orbital roof. As the frontal lobe was lifted, more adhesions were found over the left optic nerve. Around the optic nerve they were so dense that it was almost impossible to uncover the nerve. As operative dissection continued, adhesions were found to fill the entire cisterna chiasmatis. The optic chiasm was tightly adherent to the brain and could not be entirely dissected free of it. The dense matting of adhesions gave the gross appearance of a tumor lying just above the chiasm. Investigation, however, revealed that no tumor was present. So obscured were the structures by the dense adhesions that it was difficult to ascertain the normal anatomic markings in this area. In order not to overlook a second lesion in the third ventricle, as indicated by the absence of air filling this region, this structure was next explored through the corpus callosum. Through this incision the third ventricle could be seen to be wide open. The aqueduct of Sylvius could easily be visualized. A small catheter was threaded through the aqueduct for a distance of 3 inches (85 cm) without meeting an obstruction, ruling out a lesion of this structure or of the fourth ventricle.

Exploration established the presence of dense basilar arachnoiditis, which was secondary to the cranial trauma. The trauma also explained the dense adhesions between the frontal lobe and the dura and the organized subdural hemorrhagic membrane, which was less than 1 mm in thickness. A portion of the dura and the associated membrane was removed for study and proved microscopically to be an area of partially organized hematoma. The patient reacted poorly and died ten days after operation.

This patient had a typical Foster Kennedy syndrome which was found to be the result of a dense arachnoiditis extending over the optic chiasm and optic nerves and the base of the frontal lobes. No tumor was found at operation, and the dilatation of the ventricles must be attributed to interference with the circulation of the spinal fluid by the adherent arachnoid. Since exploration revealed a patent third ventricle, first and fourth ventricle. The arachnoiditis was unquestionable and of a degree capable of producing chiasmic symptoms.

#### COMMENT

Experience<sup>4</sup> has established the localizing value of the Foster Kennedy syndrome in cases of tumor of the anterior fossa. That it may be associated with conditions well removed from the anterior fossa is not so clearly recognized. It has been found in conjunction with a meningioma arising from the right side of the falx (Custodis<sup>5</sup>) and, in another instance, with a tumor of

the cerebellum in which the dilated third ventricle was held responsible for the syndrome (Cusick<sup>6</sup>). These exceptions are rare and seem to emphasize that in almost all instances a Foster Kennedy syndrome is found to be associated with a lesion of the anterior fossa in the region of the optic chiasm. To the localization of the tumor in the latter region there are also exceptions, since the syndrome has been observed with tumors of the sphenoid ridge in the parasellar region (Alpers and Groff<sup>7</sup>). In these instances however, the probability is that the tumors extended forward into the anterior fossa.

The cause of the Foster Kennedy syndrome is in most instances a meningioma. Among other causes which have been listed are tumors and abscesses of the frontal lobes, gliomas of the intracranial portion of the optic nerve and aneurysm of the internal carotid artery (Marchesani<sup>8</sup>). Kennedy<sup>9</sup> described the syndrome in case of aneurysm of the right internal carotid artery. It may be produced also by sclerosis of the internal carotid arteries.

Yaskin and Schlezinger<sup>3</sup> reported 2 cases in which the syndrome was produced by compression of the optic nerves by sclerotic internal carotid arteries. They indicated that the presence of a binasal field defect in association with the Foster Kennedy syndrome necessitated a consideration of sclerotic internal carotid or anterior cerebral arteries as the cause of the syndrome. Schloffer<sup>10</sup> reported a case which is comparable to the 2 cases mentioned. His patient had a Foster Kennedy syndrome with some constriction of the nasal fields of vision. A diagnosis of neoplasm of the anterior fossa was made. At operation a sclerotic right internal carotid artery was discovered compressing the right optic nerve. Necropsy later revealed pronounced atherosclerosis of the vessels at the base of the brain, chiefly the carotid arteries. The right internal carotid artery was so large that the compressed optic nerve was translucent. Changes

6 Cusick, P. L. Foster Kennedy Syndrome Associated with a Tumor of the Cerebellum, *Proc Staff Meet*, Mayo Clin **13** 433, 1938.

7 Alpers, B. J., and Groff, R. A. Parasellar Tumors, *Arch Neurol & Psychiat* **31** 713 (April) 1934.

8 Marchesani, O. Symptomatology des Nervus opticus, in Bumke, O., and Foerster, O. *Handbuch der Neurologie*, Berlin, Julius Springer, 1936, vol. 4, p. 58.

9 Kennedy, F. A Further Note on the Diagnostic Value of Retrobulbar Neuritis in Expanding Lesions of the Frontal Lobes, *J A M A* **67** 1361 (Nov 4) 1916.

10 Schloffer, H. Erwagungen uber die operative Entlastung des intrakraniellen Optikusabschnittes, *Med Klin* **1** 421, 1934.

4 Cushing, H. Macewen Memorial Lecture on Meningiomas Arising from the Olfactory Groove, *Lancet* **1** 1329, 1927. Schmelzer, H. Einseitige Stauungspapille und Storung des Geruchsinnes, *Klin Monatsbl f Augenh* **91** 479, 1933.

5 Custodis, E. Meningeom der Falx und lokalisiertes irreführendes Foster Kennedy'sches Syndrom, *Klin Monatsbl f Augenh* **101** 823, 1938.

on the left side were less pronounced. Schloffer concluded that atherosclerosis of the internal carotid arteries must be included in the differential diagnosis of the causation of the Foster Kennedy syndrome. He expressed the opinion that the presence of a nasal field defect should favor a diagnosis of arteriosclerotic disease of the carotid arteries rather than a neoplasm. Glees<sup>11</sup> reported 3 cases in which he believed that the syndrome was secondary to compression of the optic nerves by arteriosclerotic vessels. He offered as an explanation of the pathogenesis

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<sup>11</sup> Glees, M. Dem Foster Kennedy'schen Syndrom-ähnliche Veränderungen der Sehnerven durch Arteriosklerose, *Klin Monatsbl f Augenh* **100** 865, 1938

of the syndrome in these cases compression of the optic nerve on one side followed by local circulatory impairment in the optic nerve on the other.

#### SUMMARY

The case reported indicates that arachnoiditis of the optic chiasm and optic nerves is capable of producing the syndrome of atrophy of the optic nerve of one eye and papilledema in the other eye (Foster Kennedy syndrome) and in this respect serves to enlarge the field of possible causes in the production of this syndrome.

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# HYPERTENSIVE RETINOPATHY ASSOCIATED WITH ADRENAL MEDULLARY TUMOR (PHEOCHROMOCYTOMA)

A NEW CLINICAL ENTITY

FRANK H. RODIN, M.D.

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A review of the available literature reveals that about 35 cases of pheochromocytoma have been reported to date. Although definite ocular changes are associated with the presence of these chromaffin cell tumors, they have received little attention. Many reports failed to mention the results of ophthalmic examination, some, however, described briefly the concomitant pathologic process observed in the eye. To my knowledge, the case of adrenal medullary tumor to be reported is the first in which photographic records of the fundi were made after operation, illustrating the gradual disappearance of retinal changes. When the patient was seen three and one-half years after removal of the tumor, the retinas were normal in appearance.

Chromaffin tumors (pheochromocytoma, chromaffinoma, paraganglioma) arise from the chromaffin tissue of the embryonic sympathetic nervous system (Tassman<sup>1</sup>) and may be located in any of the paraganglia. The adrenal medulla is composed of chromaffin cell tissue, and hyperplasia of this structure probably represents the rarest form of adrenal tumor (Grollman<sup>2</sup>).

The general syndrome produced is characterized by "evidence of instability of the sympathetic nervous system, hypertension or paroxysmal hypertension, glycosuria, periodic attacks of tachycardia, vasoconstriction and vasodilatation of peripheral vessels, headaches, nausea, vomiting, sensations of constriction in the epigastrium with dyspnea, and susceptibility to shock (Labbe, Tinell and Doumer<sup>3</sup>). These authors were first to observe the phenomenon of parox-

ysmal hypertension associated with pheochromocytoma. They described the typical case as marked by periodic attacks occurring at intervals of a few hours or in response to a stimulus, such as massage of the tumor mass. During the episodes, which usually last from five to fifteen minutes, apprehension, pallor, sweating, mydriasis, hypertension and hyperglycemia are signal features. Biskind, Meyer and Beadner,<sup>4</sup> in an extensive review of 29 collected cases and 1 personal case, observed conclusively that successful removal of the tumor provides relief of symptoms in the majority of cases, particularly when supported by adequate preoperative and postoperative care.

The cells of the pheochromocytoma have been shown to produce epinephrine<sup>2</sup> or an epinephrine-like substance. This was demonstrated for the first time in the circulating blood during a crisis by Hyman and Mencher.<sup>5</sup> According to Tassman,<sup>1</sup> epinephrine secreted by the medulla is a pressor substance and is known to cause vasoconstriction, elevate blood pressure and stimulate the sympathetic nervous system. The medullary chromaffinoma, therefore, by releasing the accumulation of pressor substance into the blood stream, may give rise to attacks of paroxysmal hypertension characteristic of an epinephrine reaction. The quantity of epinephrine contained in these tumors has been measured and provides convincing evidence of the correlation between the two phenomena.

In the eyes, this situation is often manifested by changes typical of general hypertension, as follows: dilated pupils, pallor of the conjunctivas, papilledema, hyperemic disks with indistinct margins, engorged veins, irregular in caliber, thinned, conspicuously tortuous arteries.

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This study was made possible by a grant from the Columbia Foundation.

1 Tassman, I. S. *The Eye Manifestations of Internal Diseases*, St. Louis, C. V. Mosby Company, 1942, pp. 55 and 451.

2 Grollman, A. *The Adrenals*, Baltimore, Williams & Wilkins Company, 1936, pp. 333-336.

3 Labbe, M., Tinell, J., and Doumer, E. *Crises solaires et hypertension paroxystique en rapport avec une tumeur surrenale*, Bull. et mem. Soc. med. d. hôp. de Paris **46**: 982-990 (June 23) 1922.

4 Biskind, G. R., Meyer, M. A., and Beadner, S. A. *Adrenal Medullary Tumor Pheochromocytoma Cured by Surgical Intervention, Clinical Management, Analysis of All Reported Operated Cases*, J. Clin. Endocrinol. **1**: 113-123 (Feb.) 1941.

5 Hyman, A., and Mencher, W. H. *Pheochromocytoma of Adrenal Gland*, J. Urol. **49**: 755-776 (June) 1943.

with increased light reflex in the fundus, and compression of the veins where they are crossed by the arteries. Small, flame-shaped hemorrhages and star-shaped figures are not uncommon, and perivasculitis, fibrinous exudate and fine spots of degeneration may appear in the fundi. On the basis of these changes, the ischemia resulting from thinning of the retinal arteries has been suggested by Oppenheimer and Fishberg<sup>6</sup> as the cause of "retinitis albuminurica." Tassman observed occasional exophthalmos. During the height of an attack, Hyman and Mencher found that the retinal arteries were somewhat narrower than normal and that they indented the veins slightly, were rather regular in caliber and showed a bright, irregular reflex. A slight propulsive pulse was noted. In 1 of their 4 cases the fundi were normal except for moderately thinned arteries.

#### REPORT OF A CASE

Mrs. A. B., aged 31, a saleswoman, entered Mount Zion Hospital on Nov. 11, 1939. She complained of attacks of nausea, vomiting and diaphoresis associated with headaches of seven years' duration. These attacks had become severe four weeks prior to her admission. Headaches consisted of dull, diffuse pains, which lasted for several days and recurred every three or four months. These were accompanied with nausea, vomiting and diaphoresis. The attacks lasted from five to fifteen minutes. A diagnosis of migraine had been made two years previously, and ergotamine tartrate had been administered, with relief, for several months; improvement was followed by renewed episodes of increased severity, which did not respond to this medication. The patient noticed that wearing a tight girdle or stooping forward appeared to incite an attack. She was seen by my associates and me two weeks after a particularly severe episode, at this time the diagnostic impression, based on the results of physical examination (including ophthalmoscopic investigation) and laboratory tests, was that of adrenal medullary tumor. Two years previously a physician had observed a slight thickening of the retinal arteries.

The past history was irrelevant. In the interval prior to operation the only unusual observations made on physical examination were a systolic murmur, an accentuated aortic sound, slight thickening of the peripheral arteries, a tumor mass in the region of the right kidney and changes in the optic fundi. Typical attacks were produced by massaging the tumor in the right flank. These consisted in a sensation of constricting pressure in the lower part of the chest with a pounding headache, a temporary increase in the respiration rate and the pulse rate, followed by a fall to 60 or 70 a minute, a rise in blood pressure to from 260 to 290 systolic and from 150 to 180 diastolic, cold and perspiring hands and feet, and nausea and vomiting. Paroxysms subsided within five minutes, the pulse rate rose to from 90 to 100 a minute, the blood pressure fell to from 100 to 130 systolic and from 80 to 95

diastolic. The hands and feet became warm, and the patient felt exhausted. Laboratory studies showed an essentially normal condition except for hyperglycemia, glycosuria and a dextrose tolerance curve of diabetic type. There was slight tachycardia. Roentgenograms of the skull and chest were normal. Renal function was normal. Retrograde pyelograms revealed depression of the upper calices of the right kidney as if by a tumor mass and angulation of the upper end of the right ureter. Psychiatric examination showed fair stability.

*Examination of the Eyes*—Initial examination of the eyes was made on November 19, one month previous to operation. The patient gave a history of having no trouble with her eyes except during the attacks of nausea and vomiting associated with headaches. At such times she experienced pain in the eyes, especially on looking upward. Vision became impaired for near and distant objects. She had the sensation of light coming from all directions, which annoyed her. When the attacks subsided, vision returned to normal, although the eyes felt weak for a few hours afterward.

Vision was 20/20 in each eye. External examination showed that the eyes were normal. The pupils were equal in size and reacted promptly to light and in accommodation.

*Ophthalmoscopic Examination*—*Right Eye* The media were clear. The optic disk was normal in appearance and vertically oval, with well defined margin. The retinal arteries were tortuous and narrow, the relation of the diameter of the arteries to that of the veins was 1:2. The light streak was well marked, giving the arteries the appearance of being definitely pale, with narrow, red borders. The retinal veins were engorged and showed slight tortuosity. The arteries and veins were solid looking. There was definite compression of the veins where they were crossed by the arteries. Many small hemorrhages were seen throughout the retina. These did not appear to be of recent origin, some seemed to be in the process of absorption, most were flame shaped. There were numerous white patches around the macular region, principally of the soft, fluffy, cotton wool type. These appeared in the form of narrow, elongated patches, between which normal, orange-colored retinal tissue was present. In addition, there were small, round, isolated patches. The picture was suggestive of a beginning star-shaped figure around the macula. There was also a large, opaque, white spot, 1.5 disk diameters from the margin of the disk in the direction of 10 o'clock. There was likewise an area of exudate partially covering the inferior temporal artery about 1.5 disk diameters from the margin of the disk, extending to the upper margin of the inferior temporal vein.

*Left Eye* The media were clear. The upper and nasal portions of the margin of the disk were definitely blurred. The disk was normal in color. The retinal arteries showed the same changes as those seen in the right eye, except that tortuosity was more pronounced and the arterioles were narrower. Some of the arteries, especially the branches, were covered in their course by exudate. The retinal veins were similar in appearance to those in the right eye. Changes about the macula were more striking. A large, arrow-shaped opacity was present above the macula. There were many narrow, opaque, white patches pointed toward the macula, below and nasal to it. Irregular white patches were also present in the upper temporal quadrant of the retina. There were many small hemorrhages of various sizes around the macula.

<sup>6</sup> Oppenheimer, B. S., and Fishberg, A. M. Association of Hypertension with Suprarenal Tumors, *Arch Int Med* 34:631-644 (Nov.) 1924.



Fig 1—Right Eye (on the left) The optic disk is vertically oval with well defined margin The retina. arteries are tortuous and narrow, the relation of their diameter to that of the veins is 1:2 The light streak is well marked, giving the arteries the appearance of being definitely pale with narrow, red borders The retinal veins are engorged and show some tortuosity There is definite compression of the veins where they are crossed by the arteries Small retinal hemorrhages which were present did not show in the photograph There are numerous white patches around the macular region, mostly of the soft, fluffy, cotton wool type These appear in the form of narrow, elongated patches, between which normal, orange-colored retinal tissue is seen The picture is suggestive of a beginning star-shaped figure around the macula There is also a large, opaque, white spot 2.5 disk diameters from the disk in the direction of 10 o'clock An area of exudate partially covers the inferior temporal artery about 1.5 disk diameters from the margin of the disk and extends to the upper margin of the inferior temporal vein

Left Eye The upper and nasal portions of the margin of the disk are definitely blurred The retinal arteries show the same changes as those seen in the right eye, except that tortuosity is more marked and the arterioles are narrower Some of the arteries, especially the branches, are covered in their course by exudate The retinal veins have the same appearance as in the right eye Changes about the macula are more striking There is a large, arrow-shaped opacity above the macula There are many narrow, opaque, white patches pointing toward the macula, below and nasal to it Irregular white patches are also present in the upper temporal quadrant of the retina

The photographs were taken one month after removal of the tumor The retinal changes are the same as those present before the operation



Fig 2—Photographs taken two and one-half months later (three and one-half months after the operation), showing definite changes in the fundi marked diminution of the exudate, especially in the right eye, and a more normal appearance of the retinal vessels, with reduced tortuosity The arrow-shaped exudate in the left eye, pointing to the upper portion of the macula, is smaller, but still an outstanding feature of the retinal picture The margin of the left disk has become distinct

Operation was performed on December 19, one month after our first examination of the eyes. During the preoperative period repeated examinations showed no notable change in the fundi from the original observation.

The details of operation and the preoperative and postoperative care of this patient have been reported elsewhere.<sup>4</sup> The adrenal tumor was successfully removed, and after an extremely critical immediate period of convalescence and return to health the blood pressure was stabilized at 125 to 135 systolic and 85 to 100 diastolic. The dextrose tolerance curve became normal and has remained so.

Histologic sections of the specimen removed at operation revealed true pheochromocytoma, of non-malignant character. Analysis of venous blood showed approximately 0.08 mg of epinephrine per cubic centimeter. Epinephrine was not identified on quantitative examination of the tumor tissue and cystic fluid, however, the large amounts of a catechol-like substance

diameter to that of the veins was 1:2. The arteries remained tortuous and their white markings distinct. Considerable compression of the veins persisted where they were crossed by arteries. The arrow-shaped area of exudate in the left eye pointing to the macula was still present.

One year later ophthalmoscopic examination revealed a normal retina in the right eye. The retinal veins still showed some engorgement, whereas the arteries were normal, no exudate or hemorrhages were present. The left eye revealed similar improvement except for two white vertical stripes where the arrow had been.

Examination of the eyes three and one-half years after removal of the tumor revealed that the retinas were normal in appearance.

#### COMMENT

Extensive changes in the retinas, characterized by changes in the vessels, hemorrhages and



Fig 3—Photographs taken three months later (six and one-half months after the operation), showing further improvement in the retinas. Only a few white patches remain. The veins appear normal, but the arteries are still narrow, the relation of their diameter to that of the veins is 1:2. The arteries are still tortuous, with the white markings distinct. Considerable compression of veins persists where they are crossed by the arteries. The arrow-shaped opacity in the left eye pointing to the macula is still present.

recovered may be considered a precursor of epinephrine. Significant is the production by the tumor extract of marked mydriasis of the cat's eye.

One month after operation photographs of the fundi were taken (fig 1). The changes observed two months previously were still present except for possible reduction in number and size of the retinal hemorrhages.

Photographs taken two and one-half months later (fig 2) showed definite changes in the fundi: marked diminution of exudate, especially in the right eye, and a more normal appearance of the retinal vessels, with reduced tortuosity. In the left eye the arrow-shaped exudate pointing to the upper portion of the macula was smaller, but still an outstanding feature of the pathologic process in the retina. The margin of the left disk had become distinct.

Photographs taken three months later (fig 3) showed further improvement in the retinas. Only a few white patches remained. The veins appeared normal, but the arteries were still narrow, the relation of their

formation of exudate, were observed in a patient with an adrenal medullary tumor (pheochromocytoma). After removal of the tumor the ocular phenomena disappeared.

There is no definite explanation of the mechanism by which the retinal changes associated with pheochromocytoma are produced. Tassman stated that three principal explanations are given for the ocular manifestations accompanying glandular dysfunction, all have to do in some way with gradual reduction of blood supply and impairment of nutrition. First, the retinal lesions are of vascular origin and are due primarily to changes in the walls of the vessels. Second, they are due to the toxic chemical action on the retinal tissue and vessels of certain products of degeneration which are formed as the result of disease in

another organ—in the present case, the adrenal tumor. Third, a disturbance of metabolism, with breaking down of cellular elements and production of toxins, takes place simultaneously in a primary organ.

Moon,<sup>7</sup> in describing experimental epinephrine shock, stated that large quantities of the injected drug may produce such marked, prolonged arterial constriction that the tissues are deprived of oxygen. Like anoxia of other origin, this type may be expected to be followed by capillary and arteriolar atony and increased endothelial permeability. When permeability is greatly increased, whole plasma escapes, when it is only moderately increased, the smaller protein molecules (albumin) pass rapidly through the relaxed membrane and the larger ones (globulin) tend to be retained. This could account for the retinal hemorrhages and exudates observed and photographed in this study.

In my case, in addition to the adrenal tumor and the paroxysms of hypertension, the only definite observations were the changes in the retinas. It is fair to assume that these changes were produced by the liberation of increased amounts of epinephrine due to the higher activity of the epinephrine-secreting portion of the adrenal gland consistent with tumor growth.

Epinephrine under ordinary conditions exerts the same physiologic effect as sympathetic, not parasympathetic, stimulation. It acts neither on the smooth muscle fibers nor on the sympathetic nerves alone, but directly on the myoneural junction. This means that the splanchnic head is constricted by the drug and that the retinal vessels are likewise constricted. The combined effect would be hypertension and ischemia with malnutrition.

In all cases of pheochromocytoma in which an ophthalmic examination was made changes in the eyes, varying from thinning of the arteries to the extensive pathologic process described in the present case, were noted.

How can this ocular condition be classified? According to Duke-Elder,<sup>8</sup> vascular retinopathies are conditions of the eye in which to the factor of vascular sclerosis, hypertension and toxemia are added. More dramatic and generally distributed alterations ensue in the retinal tissues themselves, characterized essentially by hemorrhages and exudates. All these conditions

are dependent on and associated only with hypertension. Without it they do not occur, even in the presence of arteriosclerosis or widespread renal destruction, as when the kidney is almost entirely destroyed by tuberculosis, sepsis or neoplasia.

From both the topographic and the prognostic point of view, Duke-Elder classifies them into the following types: (1) arteriosclerotic retinopathy, (2) renal retinopathy, (3) toxemic retinopathy of pregnancy, (4) malignant hypertensive retinopathy and (5) diabetic retinopathy.

The ocular lesions in my case most closely resembled malignant hypertensive retinopathy. However, there are important differences. The malignant hypertensive type is characterized by extreme papillary and peripapillary edema. In my case there was only blurring of the margin of the left disk and no edema. In none of the cases reported was there marked papillary edema, as is seen in the malignant type. The characteristic clinical picture of intense arterial constriction, hyperemia and massive edema of the disk with profuse superficial hemorrhages and soft cotton wool exudates, was lacking. In the present case small hemorrhages and limited formation of exudate were present. The star-shaped figure which is often pronounced in malignant disease was not well developed in this case. In cases of malignant type the picture is that of acute and perilous toxemia, in my case it was one of a slowly progressing condition. The question arises whether if the adrenal tumor were not removed a retinal picture characteristic of malignant hypertension would eventually develop. The answer, of course, is lacking, as no case of adrenal tumor has been reported in which the ocular condition found in the malignant type was present.

The outstanding feature in this case was the disappearance of the pathologic condition of the retina after removal of the tumor. As a rule the picture of malignant hypertensive retinopathy is considered to be as Duke-Elder expressed it, a "death variant." There are cases observed over a long period in which renal failure did not develop and partial or complete recession took place.<sup>9</sup> These cases, however, are the exception.

7 Moon, V. H. *Shock: Its Dynamics, Occurrence and Management*, Philadelphia, Lea & Febiger, 1942, p. 48.

8 Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1940, vol. 3, pp. 2706-2729.

9 Schieck, F. *Netzhautveränderungen bei Nierenleiden und bei Blutdrucksteigerung*, in Henke, F., and Lubarsch, O. *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1928, vol. 11, pt. 1, pp. 619-630. Floyd, R. *Retinal Changes in Hypertension and in Renal Disease*, *Arch. Ophth.* 6: 433-444 (Sept.) 1931. Fishberg, A. M., and Oppenheimer, B. S. *Differentiation and Significance of Certain Ophthalmoscopic Pictures in Hypertensive Diseases*, *Arch. Int. Med.* 46: 901-920 (Dec.) 1930.

It is my opinion, therefore, that the case reported presents a retinal entity characterized by the changes in the retina, hypertensive paroxysms and the presence of a pheochromocytoma, in which the pathologic process in the retina disappeared after removal of the tumor. Such an ocular condition should be classified as a hypertensive retinopathy associated with adrenal medullary tumor.

In cases of hypertensive retinopathy with paroxysmal attacks the possibility of a coexisting adrenal tumor should always be considered.

#### SUMMARY

Pheochromocytoma is a rare form of chromaffin tumor, which is characterized by a train of hypertensive symptoms, including definite ocular changes.

Epinephrine or an epinephrine-like pressor substance is contained in the cells of this tumor.

Large amounts of this substance freed into the blood stream cause vasoconstriction, elevate blood pressure and stimulate the sympathetic nervous system, producing paroxysms of hypertension. In the eye, changes are typical of hypertensive retinopathy.

Extensive changes in the retinas, characterized by changes in the retinal vessels, hemorrhages and formation of exudate, were observed in a patient with an adrenal medullary tumor (pheochromocytoma). After removal of the tumor the ocular phenomena disappeared, as illustrated by the serial photographs. There is no definite explanation of the mechanism by which the retinal changes are produced.

I feel that the ocular condition in this case is a new clinical entity and should be classified as hypertensive retinopathy associated with an adrenal tumor.

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# CHANGES OF LABYRINTHINE EXCITABILITY IN LESIONS OF OPTIC TRACT OR EXTERNAL GENICULATE BODY

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Little is known as to whether retinal impulses are able to influence the excitability of the vestibulo-ocular reflex arc. Ohm<sup>1</sup> observed that postrotational nystagmus is different in the dark and in the light. It is, however, not clear from his experiments whether the differences observed were due to the changes in the illumination or to the influence of fixation. In experimental studies of Spiegel,<sup>2</sup> it was shown that the effect of stimulation of the occipital lobe on ocular movements is changed by a lesion of the vestibular nuclei. While horizontal conjugate deviation of the eyeballs predominated as long as the vestibular nuclei were intact, the stimulation of the occipital lobes following bilateral lesions of the vestibular nuclei produced chiefly vertical ocular movements. These experiments were interpreted as indicating that the impulses for horizontal ocular movements descending from the occipital lobe reach the nuclei of the ocular muscles after passing through a relay station in the vestibular nuclei. This corticofugal system from the occipital lobe to the vestibular nuclei could serve for conduction of impulses originating in the occipital lobe and influencing the vestibulo-ocular reflex arc. The existence of such an influence was demonstrated in further experiments by one of us with Dr Wycis,<sup>3</sup> in which unilateral destruction of the area striata was followed by differences in the postrotatory nystagmus on clockwise and on counterclockwise rotation, the postrotatory nystagmus to the side of the lesion lasting much longer than that directed to the opposite side. This phenomenon seems related to the directional preponderance observed by Fitzgerald and Hallpike<sup>4</sup> on caloric

stimulation in cases of brain tumor. It suggested that elimination of the centripetal impulses entering the area striata may have a similar effect. In order to test this possibility, experiments were performed in which the effect of unilateral lesions of the optic tract or of the external geniculate body was studied.

## METHOD

Lesions of the optic tract or of the external geniculate body were produced electrolytically in cats under pentobarbital sodium (nembutal) anesthesia, the needle being introduced by means of a Horsley-Clarke stereotaxic apparatus, or the optic tract was cut after it had been exposed by the technic of the overhanging brain developed by Karplus and Kreidl.<sup>5</sup> Postrotatory nystagmus was produced on an electrically driven rotating chair that insured uniform stimulation by 10 rotations in twenty seconds. The duration of this nystagmus and the number of jerks were determined, and their amplitude was estimated. The animals were subjected alternately to 10 clockwise and to 10 counterclockwise rotations, each series of rotations being performed three times. The cats were first tested for several days to ascertain fluctuations in the excitability, animals with marked differences on clockwise and on counterclockwise rotation being discarded. The examination was repeated on the day following the operation and subsequently at intervals of from two to three days in the first one or two weeks and later at weekly or longer intervals for periods up to four months.

## RESULTS

In principle the same changes were observed, whether the lesions were placed in the optic tract or in the external geniculate body. Similarly as in the striatal lesions, a marked difference between the postrotatory nystagmus following clockwise rotation and that following counterclockwise rotation was observed postoperatively. There was a "directional preponderance," the nystagmus directed with its fast component toward the side of the operation being distinctly more intense than that directed to the opposite side. The duration of the postrotatory nystagmus to the side operated on reached up

Nystagmus Resulting from Cerebral Lesions, *Brain* **65** 115, 1942

5 Karplus, J P, and Kreidl, A. *Gehirn und Sympathicus, Arch f d ges Physiol* **129** 138, 1909

From the Department of Experimental Neurology, Temple University Medical School, Philadelphia

1 Ohm, J. *Zur Augenzitterkunde, Arch f Ophth* **125** 245, 462 and 554, 1930, **126** 221, 1931

2 Spiegel, E A. Role of Vestibular Nuclei in the Cortical Innervation of the Eye Muscles, *Arch Neurol & Psychiat* **29** 1084 (May) 1933

3 Wycis, H T, and Spiegel, E A. Influence of Cortical Areas upon the Vestibulo-Ocular Reflex Arc, to be published

4 Fitzgerald, G, and Hallpike, C S. Observations on the Directional Preponderance of Caloric

to three times, the number of its jerks up to four times, the corresponding values of the nystagmus to the normal side, often also the amplitude of the jerks was larger when the postrotatory nystagmus to the side operated on was elicited than when the oppositely directed nystagmus was produced. On comparison with the preoperative values one found either increase of the duration and number of jerks of the nystagmus to the side operated on (see cat 128) or decrease of the nystagmus to the normal side (see cat 124) or a combination of these two phenomena. Occasionally there was an increase of the reaction to both sides, but also in such instances there was still the preponderance to the side operated on (see cat 135). The changes were often demonstrable as soon as twenty-four hours after operation, as illustrated by the following experiment

Cat 132	Postrotatory Nystagmus to Left (after 10 ↶)		Postrotatory Nystagmus to Right (after 10 ↷)	
	Duration	No of Jerks	Duration	No of Jerks
12/7/44	14 15 sec	15	12 14	14 15
12/7/44	Severance of left optic tract on overhanging brain			
12/8/44	27 30	32 41	10 13	6-12
	Amplitude of nystagmus to left definitely larger than that of nystagmus to right			
	Anatomic examination revealed complete severance of the left optic tract close to the chiasm			

In all tabulations ↶ means clockwise rotations and ↷ means counterclockwise rotations

In some cases the excitability of the vestibulo-ocular reflex arc was lowered on the first post-operative day and the phenomena of increased excitability described appeared one to two days later. This may be due partly to prolonged action of the anesthetic, partly to "shock". In this stage, some cats also showed an increased latent period of the reaction (see cat 128), indicating that increase of the latent period on testing the labyrinth may be caused by lesions of the central nervous system, while some clinicians assume that the increase of the latent period on caloric examination of the labyrinth indicates hypoexcitability of the receptor organ (Brunner<sup>6</sup>).

The duration of the "directional preponderance" chiefly depends on the extent of the lesion. While in more or less complete interruption of the centripetal impulses from the homolateral halves of the retinas a prevalence of the nystagmus to the side operated on could be observed for several months, a return to the normal values took place within a week in incomplete lesions

If one tests the labyrinthine excitability repeatedly with test-free intervals of a few days only, the influence of habituation is added to that of the operative procedure, it tends to lower the labyrinthine excitability bilaterally. If the examinations on the rotating chair are interrupted for a longer time, the excitability of both labyrinths again rises (see end of protocol of cat 128).

The described effect of elimination of retinal impulses may be illustrated by the following abbreviated protocols

Cat 124	Postrotatory Nystagmus to Left Following 10 Rotations ↶		Postrotatory Nystagmus to Right Following 10 Rotations ↷		
	Dura- tion	No of Jerks	Dura- tion	No of Jerks	
4/24/44	14 sec	21 25*	13 15	18-20	
4/27/44	Electrolytic lesion of right optic tract				
4/28/44	Questionable reaction		20 23	2 10	
			(undulations with small amplitude)		
4/29/44	6 10	4 11	4 18	15 21	
5/ 1/44	5 9	8-10	12 14	17	
5/ 2/44	11 12	13 17	15 17	16 18	
5/ 8/44	9 11	4 8	12 13	5 14	(fatigue after several tests)
5/10/44	9 13	9 13	10 12	12 14	
5/15/44	9 14	11 13	10 13	5 12	(fatigue after several tests)
5/22/44	11	7 8	10 11	9 10	
5/31/44	10	8	10 11	8 9	(labyrinth reflex easily fatigued)

\* In this as well as in the other protocols, the figures represent maximum and minimum values in three tests

Histologic examination revealed an oval area of demyelination in the dorsolateral part of the optic tract, however, the lesion is incomplete, leaving part of the fibers of the optic tract intact.

No 128	Postrotatory Nystagmus to Left Following 10 Rotations ↶		Postrotatory Nystagmus to Right Following 10 Rotations ↷		Comment
	Dura- tion	No of Jerks	Dura- tion	No of Jerks	
6/ 7/44	12 sec	15 18	11½ 12	19 22	
6/ 8/44	Puncture of left cerebrum without lesion of external geniculate ganglion				
6/ 9/44	7 13	10 21	10 14	17 20	
	(fatigue on repeated stimulation)				
6/12/44	5-7	9 10	6 9	10 14	
6/14/44	5 9	6-9	5-6	7 10	
6/16/44	5-6	4 6	6-8	8-11	
6/21/44	4 5	4 5	4 5	6	
6/22/44	Electrolysis of right external geniculate body				
6/23/44	7 10	4-6	0-13	0 4	Chemosis of lids
	(latent period 5 sec)	(slow undulations)	(latent period 5 sec)	(very small amplitude)	
6/26/44	5 8	3-5	11 16	15 22	Nystagmus immediately following rotation
6/28/44	5 6	5 6	12	14 15	Large amplitude in both directions, amplitude to left less than to right
6/30/44	3 4	2 3	10-13	11 17	
7/ 5/44	4 5	2 3	15	10-11	
7/10/44	4	4	11	12	
7/14/44	0 5	0 5	7-10	6-7	
7/19/44	4	5	7 8	6-12	
7/24/44	4-5	3-5	6-7	8-9	
8/ 7/44	3	2	8-9	9	
8/24/44	2-3	1 2	8-10	8-9	
10/26/44	7 10	8-12	10-12	12½ 13	

<sup>6</sup> Brunner, H. Allgemeine Symptomatologie der Erkrankungen des Nervus vestibularis, in Alexander, G. and Marburg, O. Handbuch der Neurologie des Ohres, Berlin, Urban & Schwarzenberg, 1924, vol 1, p 939

Histologic examination revealed nearly complete destruction of the right external geniculate body (fig 1)

Cat 135	Nystagmus to Right (after 10 rotations ↺)		Nystagmus to Left (after 10 rotations ↻)	
	Duration	No of Jerks	Duration	No of Jerks
12/28/44	7 7 5	10	7 5 9	10 12
12/29/44	5-8	5 7	5 7	3-5
1/ 2/45	5	4 6	5-7	4 5
Electrolytic lesion of right external geniculate ganglion				
1/ 3/45	20	38 40	12-14	22 26
1/ 5/45	22-25	45-46	7 9	12 16
1/ 8/45	20-24	32 39	11 13 5	21 29
1/11/45	18-22 (large amplitude)	27 30	10 12 (small amplitude)	11 23

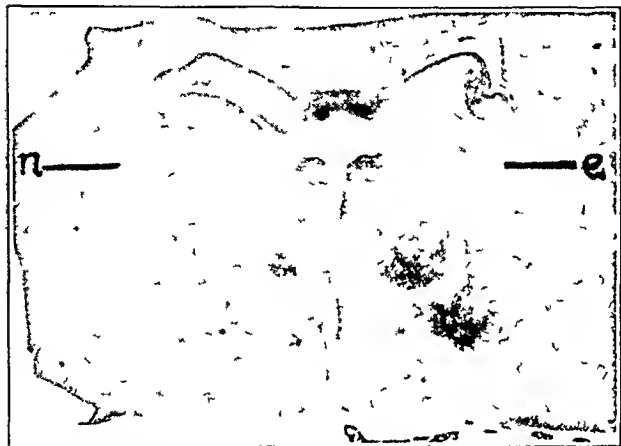


Fig 1 (cat 128)—Electrolytic lesion (e) of right external geniculate ganglion, normal left external geniculate ganglion, "n"

In control experiments punctures were performed at the same coordinates as in the electrolysis experiments, but without the electrolytic lesion. These controls showed that punctures through the parietal lobe penetrating the internal capsule (or cerebral peduncle) so that the optic tract was reached or through the white matter of the hemisphere above the external geniculate ganglion produced no directional preponderance or at the most a slight difference of a few days' duration, but never the marked long-lasting differences observed in complete or extensive lesions of the optic tract or external geniculate body.

Cat 136	Nystagmus to Right (after 10 rotations ↺)		Nystagmus to Left (after 10 rotations ↻)	
	Duration	No of Jerks	Duration	No of Jerks
1/ 8/45	12 14 sec	25 33	12 13	23-26
1/ 9/45	12 5-13	19 28	11	18 20
1/10/45	Puncture of right cerebrum, reaching right external geniculate body, without electrolysis (fig 2)			
1/11/45	13	17	7 10	8 16
	Markedly reduced reaction on repetition of test			
1/12/45	10-12	16-24	10 11	14 20
1/15/45	9 10	12-18	9 13	20-21

The postrotatory nystagmus following clockwise rotations chiefly depends on stimulation of the left labyrinth and its reflex arc to the eye muscles, the nystagmus following counterclockwise rotations on stimulation of the corresponding structures on the right side. The preponderance of the nystagmus toward the side of operation in our experiments obviously is not due to changes of excitability of the peripheral

receptor, since reflex impulses from the retinas cannot act directly on the peripheral labyrinth. They must act on parts of the vestibulo-ocular reflex arc, either on the vestibular nuclei or on the nuclei of the ocular muscles or the intercalated nuclei of the reticulate substance. This problem of the site of this interference will be approached in further studies. At present it may, however, be stated that retinal impulses seem to have a certain tonic influence on the vestibulo-ocular reflex arc. Our experiments showed that lesions of an optic tract or external geniculate body increase the postrotatory nystagmus to the same side, sometimes they also depress the nystagmus to the opposite side. These observations seem to indicate that impulses from the homolateral halves of the retinas have an inhibitory effect on vestibulo-ocular reflexes tending to produce nystagmus to the same side, while a facilitating effect on labyrinthine reflexes acting in the opposite direction is less regularly demonstrable.

#### SUMMARY

Lesions of the optic tract or of the external geniculate body were produced electrolytically in cats under anesthesia with pentobarbital sodium, the needle being introduced by means of a Horsley-Clarke stereotaxic apparatus, or the optic tract was cut after it had been exposed by the technic of the overhanging brain. A marked difference between the postrotatory nystagmus following clockwise rotation and that following counterclockwise rotation was observed postoperatively. The duration of the postrotatory nystagmus to the side operated on reached up to three times, the number of its jerks up to four times, the corresponding values



Fig 2 (cat 136)—Control experiment. Puncture of right cerebral hemisphere without electrolytic lesion of external geniculate ganglion

of the nystagmus to the normal side. This prevalence of the nystagmus to the side operated on could be observed up to several months following the operation. These observations seem to indicate that impulses from the homolateral halves of the retinas have an inhibitory effect on vestibulo-ocular reflexes tending to produce nystagmus to the same side.

# OCULAR VARICELLA

## REPORT OF A CASE OF CORNEAL PHLYCTENULE

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The ocular complications of varicella (chickenpox) are rare indeed. This impression is supported by the sparsity of the ophthalmic literature dealing with the disease. Conjunctival vesicles<sup>1</sup> exhibiting phlyctenular-like pustules<sup>2</sup> have occasionally been reported to invade the cornea. These may develop into ulcer excavations<sup>3</sup> with swollen, reddish brown margins. Minimal edema of the lids<sup>4</sup> is also frequently demonstrable.

Corneal complications are more infrequent. A direct corneal lesion is most unusual but may appear relatively late in the course of the disease. Oppenheimer, in 1905,<sup>5</sup> reported a case of a vesicular lesion which developed into a shallow ulcer. Pickard,<sup>6</sup> in 1936, reported a case of interstitial infiltration with associated endothelial changes. Rosenbaum,<sup>7</sup> in 1943, described a similar case in which was exhibited a shallow central corneal ulcer with minor infiltration of Descemet's membrane and the endothelium. Superficial keratitis has been associated with chickenpox.

In a review of the information available concerning the ocular complications of varicella several facts seem worthy of summary. (1) The ocular sequelae appear late in the course of the disease, (2) the area involved is small and circumscribed, (3) associated iridocyclitis is absent, and (4) recovery is rapid and complete. The last factor serves to differentiate the ocular changes of varicella from those of smallpox.

### REPORT OF CASE

A 30 year old resident physician at the University Hospital was first examined by us on March 10, 1942. The patient's chief complaints were diminution of visual acuity in the left eye, severe photophobia and pain.

1 Hilbert, R. *Centralbl f prakt Augenh* 26 39-41, 1902

2 Yan, C. *Klin Monatsbl f Augenh* 74 484-488, 1925

3 Sommer, G. *Wchnschr f Therap Hyg d Auges* 12 205-206, 1909

4 Pearson, A C. *Brit M J* 1 1492, 1903

5 Oppenheimer E H. *Deutsche med Wchnschr* 31 833, 1905

6 Pickard, R. *Brit J, Ophth* 20 15-18, 1936

7 Rosenbaum, H D. *Am J Ophth* 26 53-56, 1943

*Past History*—The past history was not contributory to the present illness.

*Present Illness*—The physician began to experience severe general malaise, headache and discomfort in the extremities and joints approximately sixteen to seventeen days after his son had been in contact with a patient with a moderately severe attack of chickenpox. Within twenty-four to thirty-six hours the physician's chest and trunk were involved in a rash suggestive of varicella. This was so pronounced that it closely resembled smallpox except for its polymorphous character. The temperature was 102 F the first day and 103 F the second and third days and then slowly fell, but the fever persisted much longer than usual. The lesions were excessive in number. The patient was most uncomfortable, with discomfort of the extremities and head. A minimal, but definite, degree of meningismus was demonstrable the first three or four days of the illness. On approximately the seventh day of the disease the physician noted a moderate degree of photophobia in the left eye on awakening. This became intense and uncomfortable, rapidly changing to a foreign body sensation. A minimal amount of thick mucoid discharge was experienced. The ophthalmologist was called to the home on the eighth day, at which time the results of ophthalmic examination were recorded and an artist was secured at once to reproduce the appearance of the ocular lesion.

*Ophthalmologic Examination*—Visual acuity was 6/6 in the right eye and 6/12 + 2 in the left eye. Scattered vesicular lesions were present on the face, lids and scalp. The lesions on the lids presented several stages of development, but the majority manifested purulent change. A slight amount of edema of the lids was noted in both eyes, but the swelling was more severe in the left eye. The eyes were straight in the primary position. The cover test disclosed minimal exophoria. The direct, consensual and accommodative reflexes were active and equal in the two eyes. The conjunctiva of each eye revealed several small vesicular areas, each of which possessed a small areola of hyperemia. Slight chemosis was present in both eyes. A faint pericorneal flush was noted in the left eye, being more conspicuous in the 6 o'clock meridian. There was suggestive corneal anesthesia of the left eye. The cornea of the right eye was normal except for a few scattered pinpoint areas which stained with 2 per cent fluorescein. A binocular loupe was necessary to visualize these areas. They were also present in the left eye, but, in addition there was a definite zone of infiltration 1 to 0.5 mm in diameter and 1 to 2 mm from the limbus in the 6 o'clock meridian. This area was raised and stained diffusely with fluorescein. Examination with the slit lamp revealed minimal loss of superficial epithelium over the area of infiltration, which spread diffusely into the superficial stroma for about 2.5 mm. The cornea was thickened superficially, but no deep lesions could be demonstrated.

No aqueous flare was noted in the left eye. The iris was normal in this eye. The fundus was normal in both eyes except for slight hyperemia of the disk and retina.

Therapy was supportive, consisting in the instillation of an aqueous solution of metaphen (1:2,500), 1 drop in each eye four times a day, and ice compresses to the left eye four times a day.

Under daily observation, the zone of infiltration surrounding the phlyctenular-like lesion receded rather promptly. The ulcerated surface, a small but elevated crater, assumed a brownish red color. This seemed to be the result of accumulation of cellular debris. The phlyctenule disappeared within a period of six to seven days, but a minor degree of corneal anesthesia persisted for at least ten days. There was complete recovery of visual acuity in the left eye, as well as absence of corneal scarring, one month after the onset of the ocular lesion.

#### COMMENT

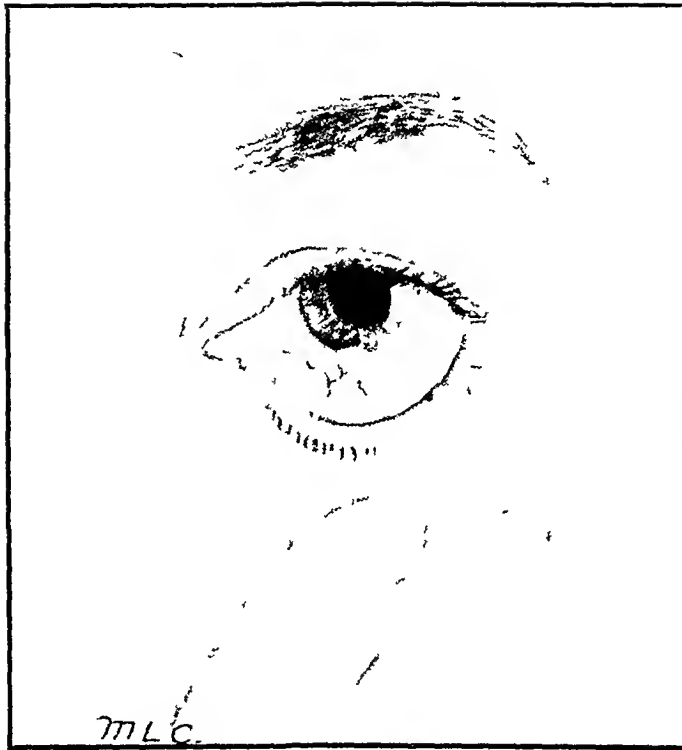
In the light of the associated corneal anesthesia, the possibility of herpetic lesions of the

cornea cannot be ruled out. The occurrence of such a complication is not completely dismissed in the literature and cannot be disproved in this case. The associated conjunctival vesicles and cutaneous lesions seem to support the diagnosis of varicella. The literature indicates a frequent association between herpes and varicella.

#### SUMMARY

Several factors revealed in the present case support similar observations mentioned in the literature: (1) the relatively late onset of ocular sequelae, (2) the small area involved, (3) the rather circumscribed character of the lesions, (4) the absence of iridocyclitis and (5) the completeness and rapidity of healing.

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Ocular lesion associated with varicella





# GONIOSCOPY SIMPLIFIED BY A CONTACT PRISM

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Examination of the angle of the anterior chamber of the human eye is shortened and simplified by the use of a contact prism which does not require unusual illuminating and microscopic equipment. The prism, which does not extend beyond the limbus, is placed directly on the cornea and is held in apposition with the cornea by pressure exerted through a flexible spring mounted on a speculum. A capillary film creates optical continuity between prism and cornea and, at the same time, lubricates the contact surfaces. Contacting surface *A* (fig 1)

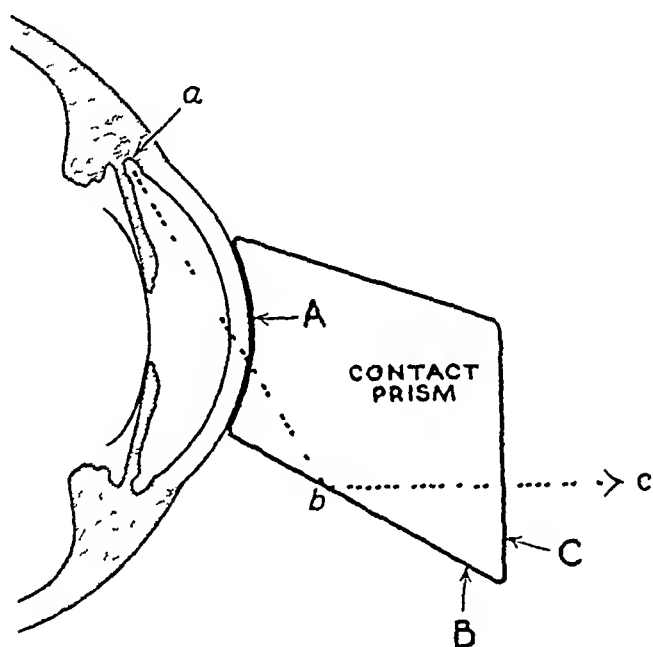


Fig 1—Cross section showing prism gonioscope on the cornea, with ray of light emerging from the angle of the anterior chamber

conforms to the curvature of the anterior surface of the average cornea. Surfaces *B* and *C* form an internal reflecting prism. A ray of light from *a* in the angle of the anterior chamber is reflected at *b* to the observer, at *c*.

The prism is pivoted and suspended by fine wire springs, *a* (fig 2 *A* and *B*), from the carriage, *b*, which rotates within a groove at the wide end of a hollow truncated cone, *c*. Extra thickness on the under side of the cone at *d* lifts the speculum above the lower lid to counteract the normal projection of the upper lid over

the cornea. The flange, *e*, conforms to the curvature of the sclera and retains the instrument by fitting under the lids. The handle, *f*, is used for insertion of the speculum, stabilizing it when the prism is rotated, and for manipulation to help in changing the angle of view into the chamber angle.<sup>1</sup>

Both prism and speculum are made of transparent plastics and, therefore, are relatively unbreakable.<sup>2</sup>

Two drops of a 0.5 per cent solution of tetracaine hydrochloride is administered to the eye which is to be examined. The patient is seated at the slit lamp biomicroscope, as for the usual examination with the slit lamp. A drop of methyl cellulose solution<sup>3</sup> is placed on the contacting surface of the prism. The speculum, with the handle below, is introduced under the upper lid while the patient looks down. Then, as he looks straight ahead, the lower lid is slipped over the flange of the speculum. The patient's head may be tilted backward to assist in lifting the upper lid and to rotate the eye to the center of the prism. The binoculars are directed and focused toward the mirror image of the chamber angle, which appears to be situated behind the reflecting surface of the prism.

The chamber angle is illuminated by the slit lamp beam. When the reflecting surface is above or below the pupil, the light beam must be directed to the desired area by the reflecting surface (fig 3 *A*). To accomplish this, the slit lamp is placed as nearly coaxial with the biomicroscope as possible. When the reflecting

1 A similar prism mounted on a flexible handle, and with an accessory magnifying surface for use with the loupe or the unaided eye, has been described. This earlier development is used similarly but is held in place by hand (Allen, L. A New Contact Lens for Viewing the Angle of the Anterior Chamber of the Eye, *Science* 99:186 [March 3] 1944).

2 Bausch and Lomb Optical Company, Rochester, N. Y., will make the prism gonioscope available.

3 The preparation used was Methocel (Dow Chemical Company). One per cent of the 4,000 centipoise type of methyl cellulose in a solution of sodium chloride, recently introduced for use with contact lenses by Kenneth C. Swan, M.D., is water soluble, nontoxic, highly transparent and lubricating. If this solution is not available, isotonic solution of sodium chloride may be substituted.

surface is to either side of the pupil, the best illumination is achieved by refracting the light beam directly through the anterior surface of the prism (fig 3B). In both these positions the slit lamp beam is kept on the same horizontal plane with the objective lenses of the biomicroscope. Transillumination through the sclera and limbus is also practical.

The angle of view is changed, in order to see behind the iris hump or to view more of the posterior surface of the cornea, by having the patient shift his eye toward or away from the reflecting surface of the prism. This change of

globe. In such instances the examiner supports the instrument by the handle with one hand while adjusting the biomicroscope with the other. This additional manipulation does not make the examination difficult or notably prolong it.

Any negative pressure (present in the use of other types of gonioscopes) between the prism and the eye is avoided by the flexible linkage of the prism to its support. There is, therefore, no distortion in the appearance of the chamber angle and no disturbance of the blood supply to the anterior segment of the eye. Optical continuity between cornea and prism is maintained.

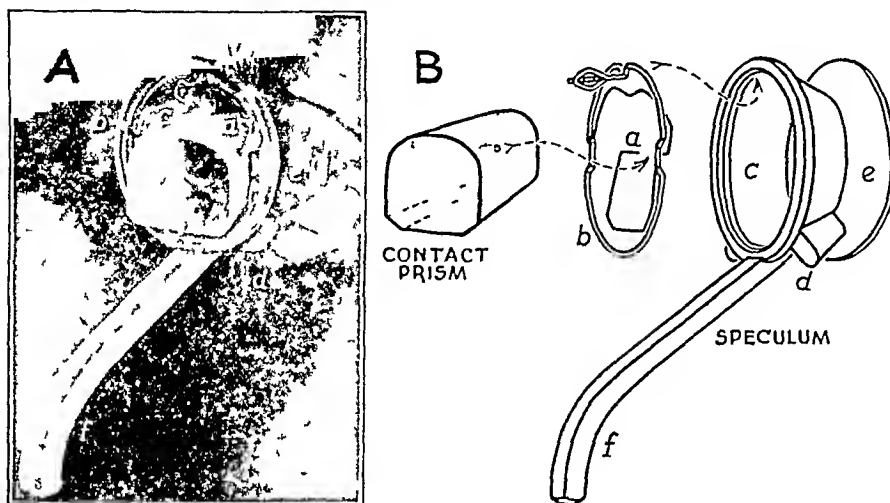


Fig 2—A, photograph of the prism gonioscope in place on the eye, B, component parts of the prism gonioscope.

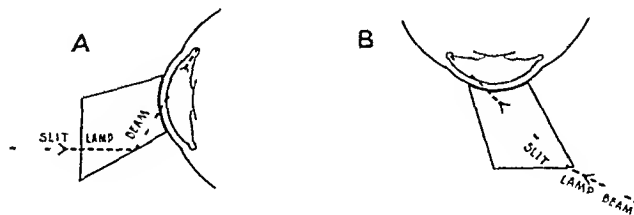


Fig 3—Illumination of the anterior chamber during examination with the prism gonioscope (A) by reflection within the prism, while the examiner is viewing the upper or lower portion, and (B) by refraction, while the examiner is viewing the lateral portions.

angle may be increased by adjusting the handle of the instrument. More than one fourth of the circumference of the chamber angle is visible with the prism in any one position. To examine other portions, the prism is rotated on the cornea.

With experience, it will be found that the entire examination time will correspond roughly to that needed for other examinations with the slit lamp.

A few cases have been encountered in which the gonioscope did not rest close enough to the

easily because of the capillary film and flexible mounting. If this continuity is temporarily interrupted, it can be reestablished immediately by shifting of the patient's eye.

None of the eyes examined has shown abrasion of the corneal epithelium resulting from direct contact of this prism with the cornea. The prism has been left on the normal eye for as long as twenty minutes without disturbance of the tissues and without apparent discomfort to the patient.

University Hospitals

# DEVELOPMENT OF SECRETORY FUNCTION OF CILIARY BODY IN THE RABBIT EYE

EVALUATED FROM ASCORBIC ACID CONCENTRATIONS AND  
CHANGES IN VOLUME

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AND

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Recent studies on the adult rabbit have indicated that electrolytes enter the anterior chamber of the adult rabbit eye as a result of a secretory process<sup>1</sup>. In order to evaluate one of the various possible etiologic factors responsible for the characteristic ocular maldevelopment in approximately 12 per cent of infants born extremely prematurely,<sup>2</sup> it seemed important to determine when the intraocular fluid assumes its adult character of a secretion.

Since the high concentration of ascorbic acid in the aqueous humor of adult animals is thought to be maintained by secretion,<sup>3</sup> one approach to the solution of the problem has been to measure the time at which ascorbic acid reaches the concentration characteristic of the adult intraocular fluid. To obtain these data, ascorbic acid concentrations in the aqueous humor were determined successively at intervals after birth and the results compared with changes in volume of the anterior chamber of the whole eye.

## EXPERIMENTAL STUDY

*Materials and Methods*—The young rabbits used in these experiments were either born in the laboratory farm or obtained within a few days after birth from a local animal dealer. They were housed with the mother until weaning. The diet of the mother consisted of Purina rabbit pellets, fresh vegetables and hay. Both food and water were allowed as desired.

From the Pathology Laboratories of the Massachusetts Eye and Ear Infirmary, and the Harvard Medical School.

1 Kinsey, V E, and Grant, W M. The Mechanism of Aqueous Humor Formation Inferred from Chemical Studies on Blood-Aqueous Humor Dynamics, *J Gen Physiol* 26 131, 1942.

2 Terry, T L. Ocular Maldevelopment in Extremely Premature Infants, *J A M A* 128 582 (June 23) 1945.

3 Friedenwald, J S, Buschke, W, and Michel, H O. Role of Ascorbic Acid (Vitamin C) in Secretion of Intraocular Fluid, *Arch Ophth* 29 535 (April) 1943.

Samples of aqueous humor were obtained with local anesthesia (tetracaine hydrochloride) by means of calibrated micropipets. These pipets were made of capillary Pyrex tubing and the shank of a no 27 hypodermic needle which was cemented into one end. On insertion of the needle through the cornea into the anterior chamber, the aqueous humor flowed into the pipet through capillary action. The volume of the aqueous humor withdrawn by means of this technic was estimated to represent over 90 per cent of that present. In the younger animals it was necessary to make a short incision in the skin in the region of the palpebral fissure in order to separate the lids before withdrawing the aqueous humor. For animals less than 2 weeks of age, several samples of aqueous humor were pooled. Samples of blood were obtained by cardiac puncture. The Mindlin-Butler micromethod<sup>4</sup> for the determination of ascorbic acid (reduced) was used for both blood and aqueous humor. For determinations of the ascorbic acid in the aqueous humor, samples of 0.010 to 0.085 cc were employed, for the determinations of the vitamin in the blood 0.1 to 0.2 cc was used. In all instances the samples of aqueous humor were placed in 5 per cent metaphosphoric acid immediately after collection. The Cenco-Sheard-Sanford photometer was used for the colorimetric determinations.

The volume of the eyes was calculated from the weights on the assumption that the specific gravity of the eye was 1.

*Results*—The concentrations of ascorbic acid in the aqueous humor and the blood of the rabbits are plotted in figure 1 as a function of the animal's age. It is apparent from the graph that the concentration of ascorbic acid increases abruptly, starting about the ninth day after birth. The concentration in the blood during the same interval remained the same, varying between zero and 2 mg per hundred cubic centimeters.

Because of low concentration of ascorbic acid and the small quantity of aqueous humor which could be obtained from eyes of rabbits less than 1 week old, it was not possible to determine accurately the concentration of the vitamin in

4 Mindlin R L, and Butler, A M. The Determination of Ascorbic Acid in Plasma. A Macromethod and Micromethod, *J Biol Chem* 122-673, 1938.

the aqueous humor of these eyes. However, it is possible to say that in none of the 3 instances in which attempts were made to analyze these samples did the ascorbic acid concentration exceed 3 mg per hundred cubic centimeters. Accordingly, it appears certain that the ascorbic acid concentration in the aqueous humor of the eyes of rabbits younger than 8 days of age does not differ significantly from the concentration in the blood.

It is noteworthy that the time at which the ascorbic acid concentration begins to increase coincides with the average age at which the adhesions between the eyelids break down and the eyes open.

In order to determine whether there is a post-natal rise of ascorbic acid in the aqueous humor of other species, a few preliminary determinations were made on the aqueous humor-blood ratio for ascorbic acid in the guinea pig. The concentration of the ascorbic acid was determined in the aqueous humor of 3 guinea pigs on the day of their birth and in the aqueous humor of 2 guinea pigs 8 days old. These concentrations were compared with those found in

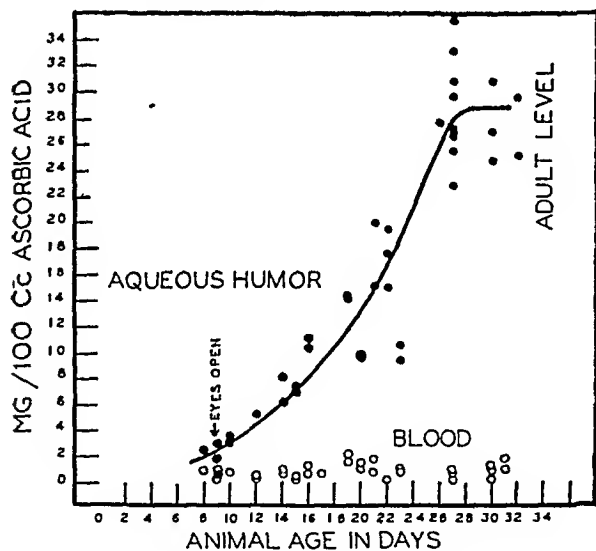


Fig 1—Chart showing the concentration of ascorbic acid in the aqueous humor and in the blood of rabbits of various ages

the mother animals. No consistent differences in the young and in the adult animals were encountered.

With the object of determining the rate at which other constituents of the aqueous humor increase after birth, the total volume of aqueous humor was determined in the eyes of rabbits of various ages. Since the eyes are growing during this period, the volumes of the eyes were also measured, so that the relative increase in the volume of aqueous humor over that

expected from the growth of the eye could be indicated by plotting the ratio of the volume of the aqueous humor to the total volume of the eye.

The volume of aqueous humor, the volume of the eye and the ratio of the former to the latter are all plotted in figure 2. It will be seen that both volumes increase linearly with the age of the animal from the first day of life, however, the volume of the aqueous humor is essentially zero at birth, whereas the volume of the eye is approximately 250 cu mm. Thus, unlike the ascorbic acid content of aqueous humor, the ratio

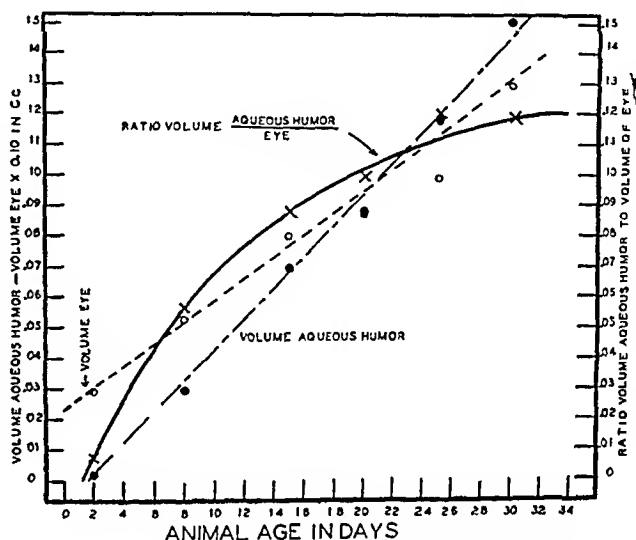


Fig 2—Chart showing the volume of aqueous humor, the volume of the eye and the ratio of these volumes in rabbits of various ages

of the volumes increases fairly rapidly during the first few days but, like the former, approaches a constant value when the animals are about 30 days old.<sup>5</sup>

#### COMMENT

The significance of the results here described may be interpreted on the basis of the studies of Friedenwald and co-workers.<sup>6</sup> They showed that the energy for secretion could be derived from differences in the oxidation-reduction potential between the epithelium and the stroma of the ciliary body. This difference in potential is due to different enzyme systems operating in the epithelium and in the stroma, the cytochrome oxidase system predominates in the epithelium.

5 The ratio of the volume of aqueous humor to the volume of the eye in adult rabbits of another series was found to be 0.105 (Kinsey, V. E., Grant, M., and Cogan, D. G. Water Movement and Eye, Arch Ophth 27:242 [Feb] 1942).

6 Friedenwald, J. S., and Stuehler, R. D. Circulation of the Aqueous. VII. A Mechanism of Secretion of the Intraocular Fluid, Arch Ophth 20:761 (Nov) 1938. Friedenwald and associates.<sup>3</sup>

and the dehydrogenase system in the stroma. Among the identified mediators of this system is vitamin C, which, according to Friedenwald, in addition to its function as a carrier of electrons to the epithelium, appears to be secreted into the anterior chamber.<sup>3</sup>

From the analyses reported on in the present paper it would appear therefore that secretion of ascorbic acid into the aqueous humor of the rabbit does not begin until approximately nine days after birth.

While the ratio of the concentration of ascorbic acid in the aqueous humor to that in the blood in guinea pigs is much lower than in rabbits, Friedenwald's experiments indicate that in general the function of ascorbic acid is the same in the two species. The few analyses which we performed on the eyes of guinea pigs suggest that secretion of this substance begins before birth. This is consistent with the well known general precociousness of this animal at birth.

Several interpretations are possible to account for the observation that the ratio of the volume of aqueous humor to the volume of the eye increases immediately after birth whereas the ascorbic acid concentration does not begin to increase until nine days later. For example, it may be assumed either that the rapid initial increase in volume is due to fluid entering the anterior chamber as a result of an ultrafiltration process or that secretion of other constituents precedes that of ascorbic acid. Until further

studies have been made, no means of distinguishing between the two explanations is apparent.

A discussion of the significance of the observations reported here with respect to early intraocular nutrition will be deferred until histologic sections are available showing the state of morphologic differentiation and maturation of the eye as a whole.

#### SUMMARY

The ascorbic acid contents of the aqueous humor and blood were measured in a series of rabbits from the time of birth until the age of 32 days. The concentration of ascorbic acid in the aqueous humor was found to increase rapidly after the ninth day, reaching the level found in adult animals approximately eighteen days later, whereas the concentration in the blood remained essentially constant. The concentration of ascorbic acid in guinea pigs at birth did not differ significantly from that in the adult animals.

Both the volume of the aqueous humor and the volume of the eye increased linearly with age from birth. The ratio of the volume of aqueous humor to the volume of the whole eye increased rapidly from the first day of life, to reach a constant value at the same time (27 days of age) that the ascorbic acid concentration reached a maximum.

Mrs Rhoda Burden<sup>1</sup> gave technical assistance in carrying out these investigations.

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# RELATION OF VISUAL ACUITY TO MYOPIA

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Although data demonstrating the relationship of visual acuity to myopia do exist, no systematic observations over a wide range of degrees of myopia have been made. For example, Laurance and Wood<sup>1</sup> give the following tabulation for degrees of myopia ranging from 0.25 to 2.50 D.

Myopia, D	2.50	2.00	1.50	1.00	0.75	0.50	0.25
Visual acuity	6/60	6/36	6/24	6/18	6/12	6/9	6/6

In a study of 1,860 white school children in Washington, D. C., Kempf and associates<sup>2</sup> found 123 with myopia ranging in degree from 0.25 to 11.00 D. The relationship of myopia to visual acuity is presented graphically (fig. 13 of that paper) by a curve which becomes asymptotic to the myopia axis at a visual acuity of 20/200. These highly improbable results are due in part to the fact that only 2 of the 123 subjects had myopia of greater degree than 4.50 D and the entire asymptotic tail of the curve, extending from myopia of 3.50 D to myopia of 11.00 D, was determined by these two points. Also of some significance in explaining these results is the fact that the largest letter on the standard Snellen chart is the 20/200 letter.

In the present study the degree of myopia and the visual acuity were determined for 64 eyes with degrees of myopia ranging from 0.50 to 13.50 D. The mean measure of myopia was 2.37 D, and the degree for 50 per cent of the subjects lay between 1.25 and 5.00 D.

## SUBJECTS AND METHODS

The subjects were students at the University of California who had consulted the optometry clinic concerning their myopia. Because the armed services reject

From the Vision Laboratory, Department of Physiology, Stanford University, Calif., and the School of Optometry, University of California, Berkeley, Calif.

Help in the statistical analysis of the data was given by Prof. Frank W. Weymouth, of the Department of Physiology, Stanford University.

1 Laurance, L., and Wood, H. O. *Visual Optics and Sight Testing*, ed. 4, Chicago, Chicago Medical Book Company, 1936.

2 Kempf, G. A., Collins, S. D., and Jarman, B. L. *Refractive Errors in Eyes of Children as Determined by Retinoscopic Examination with a Cycloplegic*, Public Health Bulletin 182, Washington, D. C., Government Printing Office, 1928.

candidates having poor visual acuity, and also because claims have been made that myopia is curable, the subjects were eager to participate in any work which might throw light on their condition. All the observers who had myopia of greater degree than 2.00 D were wearing correcting lenses.

The measure of the subject's myopia was taken as the weakest concave lens which gave a maximum visual acuity. This was checked by the use of a retinoscope. If a relatively small amount of astigmatism was present (less than 0.50 D cyl in the lower corrections, less than 1.00 D cyl in the medium corrections and less than 2.00 D cyl in the high corrections), the subject was accepted, and the "equivalent sphere" was used as the measure of his myopia. The "equivalent sphere" is the average of the spherical lenses required in the two major meridians. For example, if the correction was  $-2.00$  D sph  $\subset -0.50$  D cyl, axis 90, then the power in the 90 degree meridian would be  $-2.00$  D, while that in the 180 degree meridian would be  $-2.50$  D. The "equivalent sphere" would be the average of these two, or  $-2.25$  D.

Visual acuities from 20/10 to 20/800 were measured by the Clason visual acuity meter. This instrument, which projects letters on a screen 20 feet (6 meters) from the observer, is so constructed that the letters remain in focus while their size is varied by moving the lens system forward or backward along a track. The subject was instructed to hold a card over one eye and to watch the screen. The size of the letters at the beginning of the test was below the observer's threshold. The size of the letters presented was now increased until the subject thought he could read them. At this point he asked the operator to stop and reported what he saw on the screen. If he could read more than half the letters of a given line, this line was accepted as the measure of his visual acuity. If he could not read the letters at this point, the size of the letters presented was increased slightly, and he was allowed to try again. This procedure was repeated until the subject could read more than half the letters of any given line. The subject was instructed to try to see the letters but not to squint his eyelids, rather to keep his eyes wide open.

Visual acuities lower than 20/800 were measured by allowing the subject to approach a regular Snellen chart. Thus, if a subject walked to within 4 feet (120 cm) of the chart in order to read the 20/200 letter, his visual acuity was recorded as 4/200, or 20/1,000. This reading was then checked by allowing him to continue to approach the chart until he could read the next lower line. Thus, if he now approached to within 2 feet (60 cm) to read the 20/100 letters, his vision was recorded as 2/100, or 20/1,000. If the two readings were not the same, a third reading was taken and the three averaged. In this method of testing the subject was again instructed to keep his eyes wide open and to approach the chart until he thought he could read a given line, at which time he was to stop walking and

try to read the chart. He was cautioned against overstepping and was advised to attempt to read the letters at the farthest point possible.

## RESULTS

The visual acuity and the degree of myopia were determined in the manner described for 64 eyes. Figure 1 is a scatter diagram on a

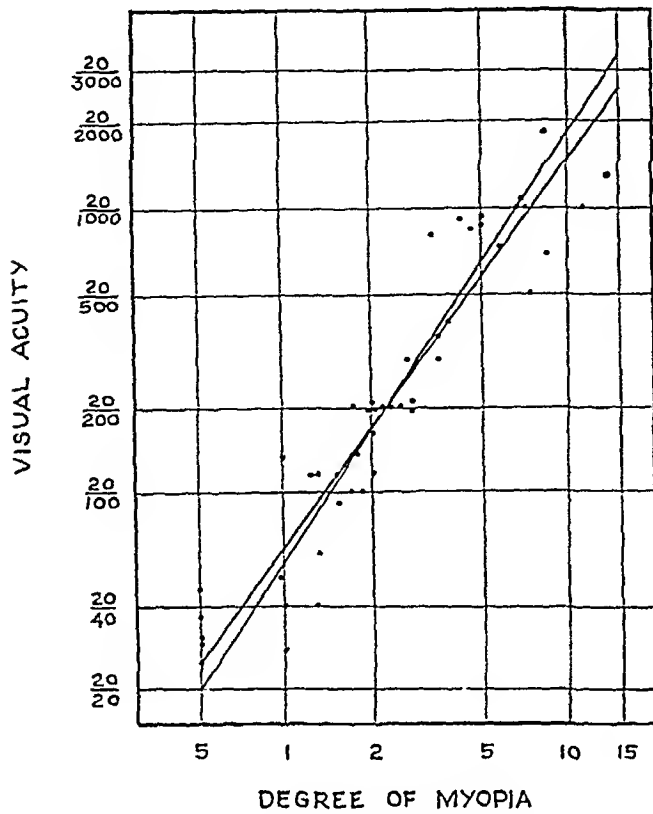


Fig 1—Visual acuity and degree of myopia plotted on a double logarithmic scale

double logarithmic scale, showing the relation between degree of myopia and visual acuity. The correlation coefficient for the relationship of the logarithm of degree of myopia to the logarithm of visual acuity is  $+0.95$ . Figure 1 also shows the regression line of the logarithm of degree of myopia on the logarithm of visual acuity and the regression line of the logarithm of visual acuity on the logarithm of degree of myopia. Each regression line has been plotted separately (figs 2 and 3) together with confidence limits of 50 and 95 per cent. If the regression lines are used for prediction, the 50 per cent confidence limits indicate the range within which one may predict and be correct 50 per cent of the time. Similarly, if one predicts that a given point will fall within the range of the 95 per cent confidence limits, the prediction will be correct 95 per cent of the time. The 50 per cent confidence limits lie at  $\pm 0.6745$  times, and the 95 per cent confidence limits at  $\pm 1.96$  times, the standard error of estimate.

The formulas for the two regression lines are

$$\log D = 1.360 \log M + 1.817 \quad (1)$$

$$\log M = 0.663 \log D - 1.169 \quad (2)$$

$M$  in formulas 1 and 2 represents the degree of myopia.  $D$  is the denominator of the Snellen fraction, and visual acuity equals  $20/D$ . Thus, a value of 80 for  $D$  represents a visual acuity of  $20/80$ , while a value of 400 for  $D$  represents a visual acuity of  $20/400$ .

The formulas may also be expressed as follows

$$D = 65.62 M^{1.360} \quad (1a)$$

$$M = \frac{D^{0.663}}{14.76} \quad (2a)$$

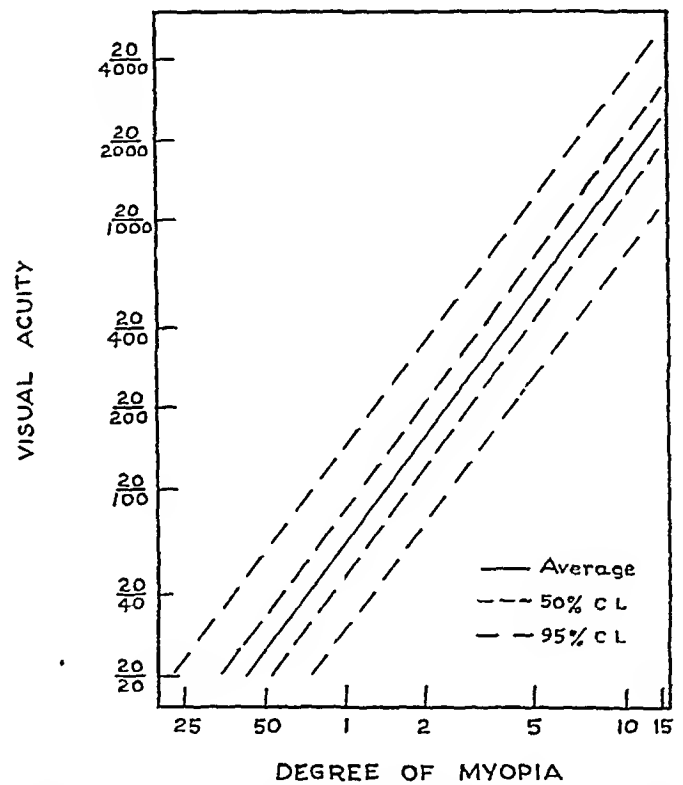


Fig 2—Visual acuities plotted for various degrees of myopia

TABLE 1—Approximate Visual Acuities for Various Degrees of Myopia

Myopia, D	Visual Acuity				
	Average	50% Confidence Limits		95% Confidence Limits	
		Maximum	Minimum	Maximum	Minimum
0.50	20/25	20/20	20/35	20/13	20/60
1.00	20/65	20/50	20/85	20/30	20/150
1.50	20/110	20/85	20/150	20/50	20/250
2.00	20/165	20/130	20/220	20/75	20/350
2.50	20/215	20/175	20/300	20/100	20/500
3.00	20/285	20/225	20/380	20/130	20/650
3.50	20/350	20/280	20/475	20/165	20/800
4.00	20/420	20/340	20/575	20/200	20/950
4.50	20/500	20/390	20/675	20/230	20/1100
5.00	20/565	20/450	20/780	20/265	20/1200
6.00	20/125	20/575	20/1000	20/340	20/1650
7.00	20/900	20/700	20/1225	20/420	20/2025
8.00	20/1100	20/850	20/1475	20/500	20/2425
9.00	20/1300	20/1000	20/1750	20/600	20/2875
10.00	20/1500	20/1150	20/2000	20/700	20/3325
12.00	20/1900	20/1500	20/2600	20/940	20/4200
14.00	20/2400	20/1850	20/3000	20/1230	20/5150

Table 1 contains the data presented graphically in figure 2. This table gives the expected visual acuity for a given degree of myopia and was calculated from equation 1. Table 2, containing the data graphically presented in figure 3, was calculated from equation 2 and shows the expected degree of myopia for a given visual acuity.

TABLE 2—*Approximate Degrees of Myopia for Various Visual Acuties*

Visual Acuity	Myopia (Diopters)				
	Average	50% Confidence Limits		95% Confidence Limits	
		Maximum	Minimum	Maximum	Minimum
20/30	0.62	0.75	0.50	1.12	0.37
20/40	0.75	1.00	0.62	1.37	0.50
20/50	0.87	1.12	0.75	1.50	0.50
20/60	1.00	1.25	0.87	1.75	0.62
20/80	1.25	1.50	1.00	2.00	0.75
20/100	1.50	1.75	1.25	2.37	0.87
20/150	1.87	2.25	1.62	3.00	1.12
20/200	2.25	2.75	2.00	3.75	1.37
20/300	3.00	3.50	2.50	5.00	1.75
20/400	3.50	4.25	3.00	6.00	2.00
20/500	4.00	5.00	3.50	7.00	2.37
20/600	4.50	5.62	4.00	7.75	2.75
20/700	5.00	6.25	4.50	8.50	3.00
20/800	5.50	6.87	4.87	9.37	3.25
20/900	6.00	7.50	5.25	10.00	3.50
20/1000	6.50	8.00	5.50	10.62	3.75
20/1500	8.00	10.50	7.00	13.75	5.00
20/2000	10.25	12.50	8.25	16.50	6.00

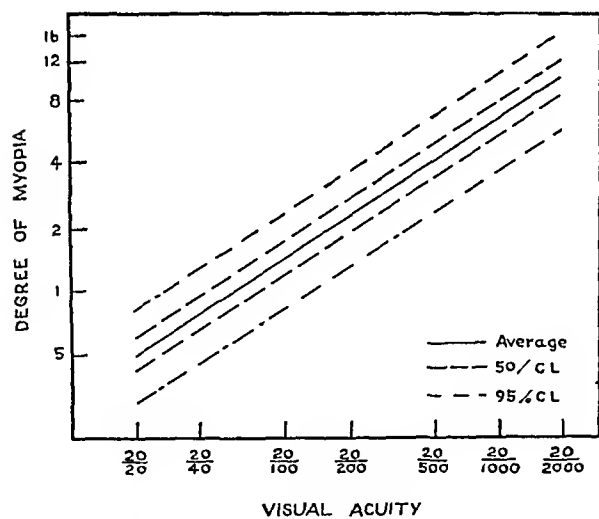


Fig 3—Degrees of myopia plotted for various visual acuties

These equations and tables are valid only for subjects similar in age to those included in this study, for similar methods of determining visual acuity and for degrees of myopia ranging from 0.50 to 15.00 D. That the equations will not hold in cases of emmetropia (with degrees of myopia below the range just mentioned) is demonstrated by substituting 0.00 for  $M$  in equation 1a. This would give a value of 0 for  $D$ , or a visual acuity of 20/0, which is of course impossible.

## CONCLUSIONS

For the homogeneous group described, visual acuity decreases in an orderly fashion as the degree of myopia increases. The relation is not linear but, rather, one fitting an exponential equation. From the tables, equations or graphs presented, it is possible to predict within certain limits either the visual acuity or the degree of myopia which may be expected if the other value is known. The following practical applications may be made of the data.

1 In clinical refraction, visual acuity is usually obtained early in the examination. Reference to table 2 will yield the expected degree of myopia and the confidence limits. If further testing (skiametric and subjective methods) shows a degree of myopia in excess of the maximum for 95 per cent confidence limits, one should suspect that the correction being determined is in fact an overcorrection of the myopia.

This is not a new idea. The old time spectacle peddler and early refractionist, who depended solely on subjective methods, used visual acuity as a determinant of the starting point of his trial and error procedure. Also, the well known rule of thumb that "minus lens may be safely added to the correction so long as each 0.25 D of concave sphere increases acuity by one line of Snellen type," is based on this same idea.

2 The use of the visual acuity fraction as a determinant of fitness for military service by the United States Army has led to many strange situations. Although many persons with 3.00 or 4.00 D of myopia have received selective service classifications exempting them from service on the basis of their myopia, others with as much as 12.00 D of myopia have been accepted by the Army. The use of the data contained in this paper will not rectify this situation as completely as would the adoption of the refractive state as a standard for selection, but it would tend to reduce the range of myopia found in acceptable candidates.

Since the minimum visual acuity for the Army is 20/400, reference to table 2 gives minimum and maximum degrees of myopia for 95 per cent confidence limits at 2.00 and 6.00 D. Thus, one may say that any person with myopia of 6.00 D or more who asserts that he can read the 20/400 letters is probably squinting or memorizing the chart. Conversely, any applicant who manifests less than 2.00 D of myopia and claims inability to read the chart solely on the basis of his myopia is probably malingering. Table 1, in which may be found the expected performance for persons with a given degree of myopia, would be a fur-

ther aid in detecting malingering, squinting the eyelids or memorization of the charts

Visual acuity is also utilized in determining employability in certain industries, and the industrial problems lend themselves to a similar analysis and solution. If a certain task requires 20/40 vision, reference to table 2 shows the minimum degree of myopia to be 0.50 D. Thus, all employees on this job who manifest more than 0.50 D of myopia should wear correcting lenses despite the fact that by memorization or squinting they are able to read the required line of the chart.

#### SUMMARY

Visual acuity and the degree of myopia were determined for 64 eyes. The subjects were all

college students whose myopia ranged from 0.50 to 13.50 D.

Plotting the logarithm of visual acuity on the logarithm of the degree of myopia gives a coefficient of correlation of  $+0.95$ .

Confidence limits were determined for the regression lines and tables set up for predicting either the degree of myopia or the visual acuity if the other is known.

These tables have value in refraction in guarding against an overcorrection of the myopia.

The data presented would also be of value in detecting malingering, squinting of the eyelids or memorization of the charts in testing personnel for military service or for employment in industry.

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# MELANOMA OF THE SKIN WITH INTRAOCULAR AND ORBITAL METASTASES

## REPORT OF A CASE

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It has been stated by Virchow that organs which are a frequent site of origin of primary cancer are prone not to have metastatic growths. Although it is now recognized that there are many exceptions to this statement, the rule seems to apply with peculiar force to the melanotic malignant growths of the eye. Most of the melanomas of this organ are known to be primary in the choroid. Only a few have been reported as metastasizing to the eye from other sites of origin. Recently there came under observation at City Hospital a patient with the unusual occurrence of a melanotic tumor arising in the skin and producing intraocular metastases. In addition, his case presented the unique feature of metastasis to the orbital tissue. This case forms the basis of the present report.

### REPORT OF CASE

*History*—A white man aged 68 was admitted to the first medical division, service of Dr Henry Marks, City Hospital, Welfare Island, on July 27, 1944, complaining of axillary pain, of five months' duration. Two years previously, a painful "strawberry" mass appeared in the skin of the right posterior wall of the chest. The growth was excised surgically, an area about 2 cm in diameter being removed. The histologic diagnosis is not available. The patient remained in good health for eighteen months. Then, at the site of the previous operation, another mass appeared, which was very painful, its appearance was soon followed by severe pain and swelling in the axilla. The axillary mass was removed, mainly for relief of pain. Histologic examination showed metastatic malignant melanoma of the lymphatic nodes. The patient also had pain in the tibia, both at rest and while walking. Shortly after the second operation, widely scattered subcutaneous masses developed over the entire body. Some nodules ulcerated through the skin and were very painful. More recently, there had been increasing weakness, considerable loss of weight and progressive loss of vision. There were no other data pertinent to his condition.

*Physical Examination*—The patient appeared extremely anemic and chronically ill. He complained chiefly of persistent pain in the right axilla. Scattered over the entire body were innumerable masses,

ranging in size from 1 mm to 1 cm. Some were subcutaneous and freely movable, and others were fixed to the skin, the largest tended to ulcerate and were reddish violaceous and painful. The scar of the first operation was bright violaceous and was surrounded by many small masses. In the axillary scar were many blue-black nodules. The left axillary lymph nodes were enlarged and painful. The chest was diffusely painful to



Fig 1—A, metastatic mass in the orbit attached to the normal optic nerve of the left eye, B, choroidal lesions beneath the pigment epithelium, and C, second choroidal focus with melanotic cells

percussion. The temperature was normal, 98.6 F, the pulse was somewhat rapid, 90 per minute, and the respiratory rate was 20 per minute. The urine contained melanin. There were no other observations of note in the general examination.

Ophthalmologic examination, made two days before the patient's death by Dr Alfred Kestenbaum, showed the following condition. The pupils reacted normally

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to light and in accommodation. The left pupil was irregular in shape, owing to a raised yellow nodule on the nasal side of the iris.

**Right Eye** The retina was detached on the nasal side to an elevation of 10 D and was gray-green. A corresponding loss of the temporal field was demonstrated by the confrontation test.

only the testes and the left epididymis being uninvolved. The ribs, vertebrae and sternum had a diffuse jet black color. The base of the skull was similarly discolored. The vault had scattered areas of pigmentation. The other bones were not examined. The cerebrum and cerebellum, dura and leptomeninges had innumerable tumors. One pigmented mass was present in the



Fig 2—A, metastatic lesions in the ciliary body, and B, metastatic lesion in the iris

**Left Eye** A detachment similar to that observed in the right eye was seen on the temporal side.

**Course**—The patient failed rapidly and died on the sixth day in the hospital, of cardiac failure and terminal pneumonia.

**Autopsy** (performed two and a half hours after death) —There were widespread metastases in the organs,

pituitary. A smear of the heart blood showed melanoma cells.

Only the left eye was removed. In the orbital fat on the nasal side was a roughly globular white mass, lightly attached to the optic nerve by fine fibrous adhesions (fig 1 A). Externally the eye was normal. On section, a gray-black mass was seen to occupy the posterior part of the globe about the nerve head, reach-



ing the equator of the bulb on the midtemporal and inferior sides. The tumor was situated in and completely replaced the choroid. It consisted of groups of polyhydral cells in a well vascularized connective tissue. The nuclei were hyperchromatic and varied greatly in size, shape and staining reaction. Cytoplasmic melanin was usually abundant, a few cells appeared devoid of it. Over the summit of the mass, the pigmentary layer of the retina was closely apposed (fig 1 B), the nucleated layers being detached by a slight amount of subretinal fluid. At the reflected edges of the tumor the retina was not detached. Extending anteriorly within the choroid, as far as the ora serrata, small masses of melanotic cells were present (fig 1 C). The ciliary body had areas of diffuse involvement by similar pigmented cells (fig 2 A). In the iris, several similar small masses were situated beneath the anterior limiting membrane (fig 2 B).

The orbital mass presented a slightly different appearance. The malignant cells tended to be larger, more separated and more anaplastic and had much less pigment than those in the bulb. The individual nests were surrounded by a fine membrane, similar to the basement membrane of a gland and producing a close resemblance to gland formation. The optic nerve was not invaded.

**Diagnosis**—The diagnosis was primary malignant melanoma of the skin with extensive metastases, including intraocular and orbital foci.

COMMENT

Metastatic melanomas of the eye are extremely uncommon. In a review of the medical literature only 7 acceptable cases were found. The first was reported by Schiess-Gemuseus and Roth,<sup>1</sup> in 1879. This report was followed by the communications of Lauber,<sup>2</sup> and Adamuk,<sup>3</sup> which dealt with the same case. Later were the cases reported by Ten Doesschaate,<sup>4</sup> Cordes and Horner,<sup>5</sup> Corrado,<sup>6</sup> Fry,<sup>7</sup> and Kreibig.<sup>8</sup> The data are summarized in the accompanying table.

In Bromser's<sup>9</sup> case histologic examination of the tumor of the skin, which he considered the primary focus, was not made, and his conclusion was questioned by Fuchs.<sup>10</sup> The case of

Pfluger<sup>11</sup> may be authentic, but complete confirmation is lacking.

According to de Schweinitz,<sup>12</sup> tumors of the eye of metastatic nature are characterized by certain features. They tend to be multiple, flat and bilateral. Certain areas of the eye are usually affected. The tissues surrounding the foci are comparatively healthy. The neighboring blood vessels frequently have malignant cells in the lumen. The last criterion must be accepted with some reservation, since this is a feature even of primary malignant melanoma and is also displayed by some carcinomas.

The present case presents many features displayed by the cases previously reported. The site of origin was the skin, similar to that in 6 of the 7 cases in the literature. All the characteristics mentioned by de Schweinitz were likewise present. The orbital metastasis found

Data on Cases of Metastatic Melanoma of the Eye

Author	Site of Origin	Sites of Metastasis
Schiess-Gemuseus and Roth, <sup>1</sup> 1879	Skin	Papilla and optic nerve
Lauber, <sup>2</sup> 1907	Lids and conjunctiva	Uveal tract
Adamuk, <sup>3</sup> 1909		
Ten Doesschaate, <sup>4</sup> 1921	Opposite eye	Uveal tract
Cordes and Horner, <sup>5</sup> 1930	Skin	Right and left iris both ciliary bodies optic nerve
Corrado, <sup>6</sup> 1931	Skin	Ciliary body
Fry, <sup>7</sup> 1933	Skin	Choroid
Kreibig, <sup>8</sup> 1935	Skin	Choroid
Lisa and Givner, 1945	Skin	Choroid, ciliary body, iris, orbit

in our case is a unique feature, not previously reported with melanoma. Willis<sup>13</sup> cited 3 instances of secondary growth involving the orbit and reported 1 of his own, but none of the tumors were of melanotic nature. The cases reviewed suggest that, although most melanotic tumors of the eye are primary, the possibility should be borne in mind that they are secondary and careful search should be conducted for other primary sites and for evidence of multiple metastases.

SUMMARY

A case of primary malignant melanoma of the skin with intraocular and orbital metastases is reported. The literature is reviewed.

108 East Sixth Street

1 Schiess-Gemuseus and Roth, M. Arch f Ophth 25(pt 2) 177, 1879  
2 Lauber, H. Ztschr f Augenh 19 132, 1907  
3 Adamuk, V. Ztschr f Augenh 21 505, 1909  
4 Ten Doesschaate, G, abstracted, Klin Monatsbl f Augenh 66 766, 1921  
5 Cordes, F. C, and Horner, W. D. Metastatic Melanoma of Both Eyes, J A M A 95 655 (Aug 30) 1930  
6 Corrado. Cancro 2 87, 1931  
7 Fry, W. E. Metastatic Sarcoma of Choroid, Arch Ophth 9 248 (Feb) 1933  
8 Kreibig, W. Ztschr f Augenh 87 265 1935  
9 Bromser, cited by Leber. Arch f Ophth 31 111, 1885  
10 Fuchs, cited by Cordes and Horner

11 Pfluger, E. Arch f Augenh 14 129, 1885  
12 de Schweinitz, G. E, in discussion on Fry.  
13 Willis, R. A. The Spread of Tumours in the Human Body, London, J & A Churchill, Ltd, 1934 p 412

# CONGENITAL BILATERAL SUBLUXATION OF THE LENS

## REPORT OF A FAMILY

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Partial dislocation of the lens presents a definite problem both for the patient and for the surgeon. Recently, Clapp<sup>1</sup> reported on a family with ectopic lenses in which 8 out of 11 children showed this defect. Burch<sup>2</sup> gave a rather complete report of cases of ectopia of the lens, some of which the additional feature of arachnodactyly was presented. Attempts to improve vision in cases of partial dislocation of the lens frequently have met with failure. Clarke<sup>3</sup> expressed the opinion that the best treatment was removal of the lens. This usually involves the use of a loop, with more or less loss of vitreous, as pointed out by Duke-Elder.<sup>4</sup> Knapp<sup>5</sup> stated the belief that the most satisfactory way to remove the lens is by needling—two needles being used, one to impale the lens and the other to produce a rent in its capsule. He stressed the fact that the lens capsule is singularly difficult to puncture, being easily stretched, and that the lenticular material is only slowly absorbed.

The following case of bilateral subluxation of the lens is of interest because of the family history.

D. G., a 6 year old girl, was first seen on June 27, 1944. The patient was in a sight-saving class at that time and was brought for examination in an effort to learn whether vision might be improved.

The child was rather thin but showed no evidence of arachnodactyly. Vision was 10/200 in the right eye and 3/200 in the left eye. External examination showed that the eyes were normal except for exophoria of 14 D and a near point of convergence of 120 mm.

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1 Clapp, C. A. A Report on a Family with Ectopic Lenses, *Am J Ophth* **27** 738-740 (July) 1944.

2 Burch, F. E. Association of Ectopia Lentis with Arachnodactyly, *Arch Ophth* **15** 645-679 (April) 1936.

3 Clarke, C. C. Ectopia Lentis. A Pathologic and Clinical Study, *Arch Ophth* **21** 124-153 (Jan) 1939.

4 Duke-Elder, W. S. Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3, pp. 3241-3242.

5 Knapp, A. Operative Treatment of Congenital Subluxation of the Lens, *Arch Ophth* **27** 158-160 (Jan) 1942.

The pupillary reaction was normal, but iridodialysis was present in both eyes. The intraocular tension appeared normal on palpation. Both lenses showed subluxation, with displacement upward and inward. With the pupils dilated the zonular fibers were seen to be in place below. The lenses were transparent and showed a few fine pigment granules on their anterior surfaces. Examination of the fundus was unsatisfactory even when the pupils were dilated, owing to the position of the lenses. Retinoscopic examination was impossible, and manifest refraction did not result in improvement of vision.

The past history was without significance. Birth had been at full term, and there was no evidence of developmental anomalies other than those found in the eyes.

Operation was performed on July 10, 1944, needling being done on the right eye, with the two needle technique. As little apparent change was produced, the procedure was repeated on Oct. 16, 1944. Since, the lens has become progressively more opaque and is beginning to shrink.

*Family History*—The family history is of extreme interest.

Maternal Grandfather M. M. was seen in the Vanderbilt Clinic on April 17, 1935, at the age of 56. He gave a history of having been struck in the right eye twenty days before, with resulting loss of vision. Vision had always been poor in both eyes. On examination, vision was 20/200 in the right eye and was limited to counting fingers at 3 inches (7.5 cm) in the left eye. The right eye was normal externally, and tension was 25 mm Schiøtz. The lens was partially dislocated downward, and the zonular fibers were visible with the corneal microscope. The left eye was congested, with a tension of 38 mm Schiøtz. The lens was dislocated and lay in the anterior chamber, and, with the patient lying on his back, it would recede through the dilated pupil. On April 19, 1935 a loop extraction was done without iridectomy. After this, with a correction of +1.50 D sph  $\subset$  +5.00 D cyl, ax 8, vision was 20/50+ in the left eye (an addition of a +3.00 D sph was given for near vision).

On Nov. 26, 1936 a preliminary iridectomy was done on the right eye, with uneventful recovery. Examination on Jan. 13, 1937 showed that the lens had settled back into the vitreous. No operation was attempted. Vision was 20/30-2 in the right eye, with a correction of +6.25 D sph  $\subset$  +1.50 D cyl, ax 180. An addition of a +3.00 D sphere gave good near vision.

The patient appeared in the clinic on June 13, 1938, with the complaint of poor vision in the left eye. Vision was 20/40 in the right eye and 20/200 in the left eye. The lower half of the retina of the left eye was found to be detached. On June 20, 1938 a diathermy operation was done on the left eye, with an unsuccessful result. The patient was last seen in March 1939.

Mother M. G. was seen in the Vanderbilt Clinic on Nov. 13, 1935, at the age of 27. Vision was 20/200 in

each eye, and both lenses were partially dislocated upward and nasally. The intraocular tension was normal. On Dec 2, 1935 a needling was done on the right eye. Recovery was uneventful, but little effect was produced. A through and through needling was done on Feb 10, 1936. Absorption of the lens progressed slowly. A third needling was done on October 19. After this, the lens gradually disappeared. Vision became 20/50 with a + 10.50 D sphere.

The patient was last seen on June 24, 1944. Vision in the right eye was then 20/70. There remains some old cortex, but no further operation is desired. Near vision is good with a + 5.00 D sphere clipped on. The left eye now shows exotropia of 96 D.

Maternal Aunt A. M. was first seen in the Vanderbilt Clinic on April 17, 1935, at the age of 12. Vision was 20/100 in each eye. Both lenses were partially dislocated upward and nasally. On July 8, 1935 a needling was done on the left eye. Absorption of the capsule was slow. Improvement in vision was obtained with the following correction:

Right eye + 13.50 D sph  $\subset$  + 1.50 D cyl, ax 130, vision 20/40

Left eye + 14.00 D sph vision 20/40

The patient was last seen on Sept 16, 1944, when vision was 20/30 in each eye. She wears a + 13.75 D sphere with each eye. The lens of the right eye is unchanged. The lens of the left eye shows an old membrane and is partly opacified. The intraocular tension is normal. This patient does not like her glasses, nor does she desire further surgical treatment. Manifest refraction revealed no further improvement in vision.

#### SUMMARY

A case of bilateral subluxation of the lens in a child is presented in which 3 other members of the family had the same disease, three generations being represented. Operation was performed on all these persons. In 1 patient the condition was complicated with glaucoma due to the misplaced lens and by later detachment of the retina in that eye. In all but 1 patient the result of operation was unsatisfactory, and even in this patient complete absorption of the lens has never taken place.

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# COMPLICATIONS INCIDENT TO SIMPLE INTRACAPSULAR EXTRACTION

## SOME PROCEDURES DESIGNED TOWARD PREVENTION

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Intracapsular extraction with preservation of the round pupil is subject to the complications that occur with most cataract operations. Some of these complications are less frequent and less severe, but involvement of the vitreous and iris takes on added significance, and it is the frequency or infrequency of this involvement that determines the success or failure of this procedure.

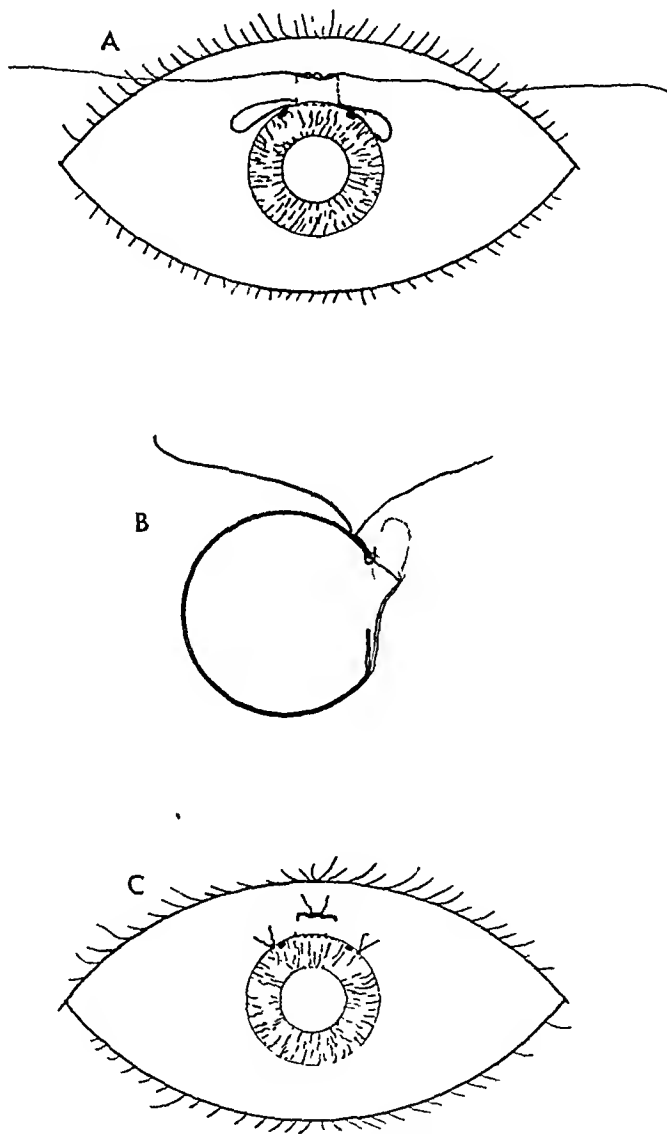
The best defense against the more troublesome complications peculiar to this operation is well placed sutures which insure adequate closure of the incision. In my experience, corneal sutures are more easily placed before opening the globe.

I have used a simple form of mattress, or section halter, suture for the past ten years which I have found very effectual, and I shall describe it briefly.

Prior to section, the globe is fixed with the globe fixation forceps, and a 24 inch (1.56 cm) silk suture double-armed with Kalt needles is inserted in the superficial stroma of the cornea just below the limbus, above, for a distance of 4 or 5 mm. After the corneal incision, which is made with a narrow conjunctival flap, the suture is completed by grasping the episcleral fibers and the conjunctiva immediately above each end of the corneal suture with the needle point suture forceps, and each needle is passed through deep episcleral tissue and brought out through the conjunctiva 5 or 6 mm above the incision. A loose horizontal knot is now made. This corneal controlling suture can be tightened, instantly closing the wound at any time, a provision which is invaluable with unruly patients or in the case of sudden prolapse or herniation of the vitreous at or near the end of delivery of the lens. This suture has the value of two sutures in the upper part of the section, but without additional sutures the wound will not immediately become aqueous tight and the chamber will not hold when refilled. I make a practice of using at least two additional corneoscleral or corneoepiscleral sutures at the positions of 10 and 2 o'clock.

### RUPTURE OF THE CAPSULE

The delicate procedure of dislocation and removal of the lens in its capsule does not depend on the forceps or the method applied. It depends on delicacy of touch and grasp, which must be



Sketches illustrating (A) conditions just prior to dislocation of the lens, with suture in place and section and iridotomies completed, (B) use which may be made of this suture when there is fear of prolapse of the vitreous (the suture is drawn to bring the corneal flap against the emerging lens), and (C) completed closure of the wound, with all sutures tied.

acquired by observation and experience before one can grasp the lens and use sufficient traction to rupture the zonule without tearing the capsule.

Most ruptures of the capsule are caused by pinching the blades too tightly, by grasping an insufficient amount of capsule or by applying too much traction before rupture of the zonule has taken place

The site for application of the capsule forceps is controversial and must be determined by the individual surgeon. Knapp's<sup>1</sup> well known method of grasping and dislocating the lens has been adopted by many surgeons. Smith<sup>2</sup> stated that to Arnold Knapp belongs the credit of showing the world how to use a capsule forceps properly. Verhoeff,<sup>3</sup> Kirby<sup>4</sup> and others grasp the capsule near the equator, above. Kirby<sup>4</sup> cited several disadvantages of grasping it below.

In my experience, few capsules tear if a wide grasp is made well down behind the iris. This permits traction to be applied to a very limited area. In pressing the Smith hook on the limbus over the point of traction, rupture of the zonule can be started without too much traction or injury to the ciliary body. After rupture of the zonule has begun, the remaining fibers separate easily, but not easily enough to permit pulling the tumbling lens up through the pupil. To avoid tearing the capsule, the major force in the maneuver must be supplied by the hook, with forceps traction as the guiding force. However, when a broken or greatly weakened zonule is indicated by extrusion and reextrusion of the iris immediately after section, it is less hazardous to grasp the lens in its upper third and deliver it head on, sliding the cataract from the eye. If the capsule should rupture before the zonule is broken and a great part of the capsule be removed with the forceps, the nucleus and the lens matter can be expressed and irrigated and removed from the chamber, and the procedure becomes a simple extracapsular extraction. However, after rupture, if the capsular opening is small, with the probability of considerable cortex remaining encased behind the anterior capsule and the contracted pupil, a complete iridectomy should be done, and the lens matter should be removed. Rupture of the capsule after the zonule is broken usually comes toward the end of delivery, and if the hyaloid membrane has not ruptured, the capsule fragments can be carefully removed. If not easily seen, they show up well with gentle irrigation.

#### RUPTURE OF THE HYALOID MEMBRANE AND PROLAPSE OF THE VITREOUS

Rupture of the hyaloid membrane and prolapse of the vitreous call for a complete iridectomy. I am in accord with Kirby<sup>5</sup> and Dunnington<sup>6</sup> in that a complete iridectomy should be done in cases in which loss of vitreous is anticipated. I must admit I have not always followed this rule. In a few cases of fluid vitreous, in which loss of vitreous was small, I endeavored to preserve the round pupil. In most of these cases the results were gratifying. The vitreous receded behind the iris, and the eyes function and appear as well as eyes in which this complication did not occur. In a few other cases the only complication was a decentered pupil, with a thin, transparent, striped band extending through the pupil, over the iris, to the point of incarceration in the section, with practically no interference with vision.

With the round pupil operation, prolapse of the vitreous, no matter how small, is a complication of importance. While a complete iridectomy does not eliminate all the unpleasant sequelae, it greatly reduces the reaction on the part of the iris and the ciliary body.

#### PROLAPSE OF THE IRIS

A securely closed wound is the greatest defense against prolapse of the iris. I performed this operation for several years without the use of sutures, depending entirely on a large conjunctival flap. I then used conjunctival sutures for a time, but, in my experience, they gave no additional security. Actual prolapse occurred in only 7 per cent of these cases, but in a number of instances there were varying degrees of peripheral incarceration or anterior adhesion of the iris to the wound. This was evident only on close inspection and caused no postoperative interference with healing or function. However, within the last year tension has developed in 2 of these cases, almost ten years after extraction of the lens. Often this adhesion of the iris to the incision is the first step in prolapse and is unavoidable in a number of cases unless the wound is made water tight or aqueous tight and the iris and the cornea are separated by a filled chamber shortly after completion of the operation. After the sutures just described are

1 Knapp, A. *Arch Ophth* **44** 1, 1915

2 Smith, H. *Arch Ophth* **55** 218, 1926

3 Verhoeff, F. H. *Tr Am Ophth Soc* **25** 1927

4 Kirby, D. B. *Am J Ophth* **27** 124, 1944

5 Kirby, D. B. *Prevention and Handling of Complications Arising During and After Cataract Extraction*, *Arch Ophth* **25** 866 (May) 1941

6 Dunnington, J. H. *New York State J Med* **44** 2224, 1944

tightened and locked and I have made certain that the iris is in position, I fill the chamber with saline solution

In some cases the patient has had violent nausea or has fallen out of bed without opening the wound, on the other hand, I have found a prolapsed iris when there was no report of disturbance. But if a wound is closed securely enough to hold the chamber, prolapse seldom develops except through direct trauma

A minor detail, which saves trouble at times, is the position of the iridotomy or the peripheral iridectomy. If the opening is made in the mid-position above, it is often difficult to disengage and unfold the iris from the wound, where it has been folded back during delivery. Placement of the iridotomy at 10 and 2 o'clock, leaving the most dependent part of the iris whole, simplifies the process of stroking the iris down into place and lessens the danger of rupturing the hyaloid membrane

Another detail which may escape notice is wedging or tucking of a narrow fold of iris into the iris angle during section. This fold is easily freed before dislocation of the lens but is frequently difficult to disengage afterward

It has been my experience that the earlier the operation for prolapse of the iris is performed, the more easily the tissue is replaced or the more cleanly it is excised, as conditions demand. Secure sutures do not give way, and replacement or excision is not the hazardous procedure of a few years ago

It is generally agreed that if the prolapsed portion contains vitreous, excision is imperative. If the prolapse is large enough to involve the pupillary margin, a small iridectomy is expedient. However, when the prolapsed portion is small and is easily replaced in the chamber, a small peripheral iridectomy, with an additional suture placed at the site of extrusion, completely restores closure of the wound and the position and action of the pupil

#### HEMORRHAGE INTO THE ANTERIOR CHAMBER

Hemorrhage into the anterior chamber is a fairly frequent complication of all cataract operations. In the intracapsular operation, with the iris intact, the possibility of a hemorrhage attaining sufficient size to rupture the wound and then to extrude the iris has to be considered. It is generally agreed that the usual source of the hemorrhage is the episcleral vessels under the

conjunctival flap. However, the iris is occasionally the source, particularly in the diabetic patient

Corneoscleral suturing has materially reduced the frequency and the amount of hemorrhage. McLean,<sup>7</sup> Kirby,<sup>5</sup> Stallard<sup>8</sup> and others have reported fewer hemorrhages with use of the corneoscleral sutures. Suturing has definitely reduced this complication, but I still find hemorrhage in about 10 per cent of cases. However, the majority of such hemorrhages are smaller than formerly. One of the greatest benefits derived from suturing is that even with the large hemorrhages substantial sutures hold fast, the wound does not gape and the blood which escapes from the chamber oozes out slowly so that the iris is practically never carried into the wound. In several cases in which the blood has filled the chamber and elevated the tension, the hemorrhage produced great pain without rupturing the sutures or causing prolapse of the iris

Removal of sutures is a delicate procedure, and unless it is so regarded hemorrhage and rupture of the wound result. I have found O'Brien's method of lid block most helpful in quieting the extremely nervous patient for removal of sutures. When the lid cannot be closed, there is not the tendency to rotate the eye upward, and the nervousness diminishes greatly

The treatment of hemorrhages, large and small, is the same and has been well summed up by Dunnington,<sup>6</sup> who stated that the vast majority of patients with this complication need little more than rest, atropine, time and patience

#### DELAYED RESTORATION OF THE ANTERIOR CHAMBER

Delayed restoration of the anterior chamber is the result of faulty closure of the wound or inefficient wound toilet

With the intracapsular operation, the iris must be carefully replaced in the globe before the sutures are tightened. If a capsulotomy has been performed, the lens matter and shreds of capsule must be irrigated and removed from the chamber. If this is carefully done and the sutures are placed into structural tissues, the anterior chamber will be reformed and virtually normal in depth a few hours after operation

In routine dressing of the wound the morning after operation I have found extreme shall-

7 McLean, J. M. New Corneoscleral Suture, *Arch Ophth* 23:554 (March) 1940

8 Stallard, H. B. *Brit J Ophth* 22:269, 1938



lowness or absence of the chamber in less than 0.28 per cent of cases since employing corneoscleral sutures

In my opinion, the necessity of secure closure of the wound cannot be too strongly stressed. It is one of the most important requirements for success with the round pupil operation. Although this calls for patience and care in the

suturing, the results gained are gratifying. Immediate restoration of the chamber is obtained, which virtually eliminates peripheral synechia, prolapse of the iris, adhesions between the hyaloid membrane and the posterior surface of the cornea, epithelization of the anterior chamber and early secondary glaucoma.

55 Park Avenue

## Clinical Notes

### INSTRUMENTS FOR USE IN OPERATION FOR CATARACT

#### An Anterior Chamber Irrigator and Two Forceps Modified for Suturing

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The anterior chamber irrigator has been used by me for ten years. The two forceps are simple modifications of instruments long in use.

#### ANTERIOR CHAMBER IRRIGATOR

The anterior chamber irrigator is a curved, flattened cannula, slightly thicker than an iris repositor, and is fitted with a rubber bulb. The posterior lip of the cannula is extended slightly to avoid picking up the iris when one is aspirating blood or air from the chamber. Free blood, iris pigment or foreign matter can be irrigated or aspirated from the chamber through a very narrow opening. This instrument may frequently be used as an iris repositor and is indispensable for refilling or inflating the chamber after the cataract incision has been securely closed with sutures.

#### GLOBE FIXATION FORCEPS

The globe fixation forceps is a fairly heavy instrument. The shafts are widely separated, so that the globe may be grasped in its entirety. Each shaft may be mounted with two teeth, or there may be the usual two and one. These teeth leave the shaft at almost a right angle. They must be very sharp at the point and broaden rapidly, so that they readily penetrate the conjunctiva and engage the sclera without

piercing it. Piercing the sclera is most improbable if the needle pressure is always exerted toward a double-toothed shaft.

The chief use of this forceps is in fixing the globe rigidly for the insertion of corneal and scleral sutures prior to section. The globe is grasped with the teeth engaging the sclera temporally and nasally about 6 mm back of the limbus. By slightly closing the forceps and at the same time pressing backward, the operator can hold the globe very steady. Deep corneal and scleral sutures may be inserted without tearing the conjunctiva, causing conjunctival hemorrhage or in any way marring the field of operation.

#### CORNEOSCLERAL SUTURE FORCEPS

The corneoscleral suture forceps is not unlike a miniature Elschning forceps. The round teeth are needle sharp and leave the shaft at an angle of 135 degrees. This forceps enables the operator to grasp the beveled edge of the corneal section and hold it fast without injuring the tissue. The teeth must be needle sharp and set at an angle that enables the operator to pick up the episcleral fibers above the section without pressing the open globe appreciably. The round teeth are an important feature of this instrument, for when teeth are so small they easily cut the tissues if they have sharp edges.

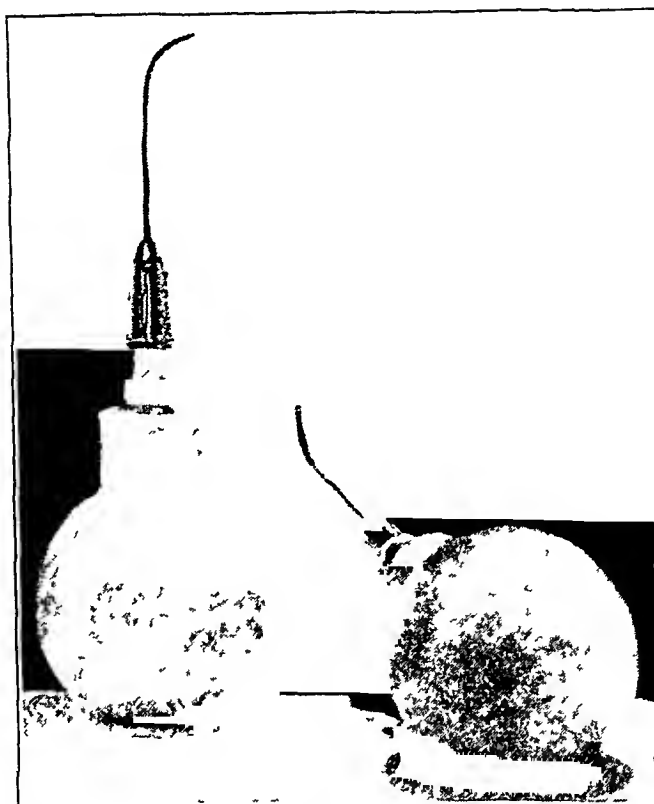


Fig 1—Anterior chamber irrigator

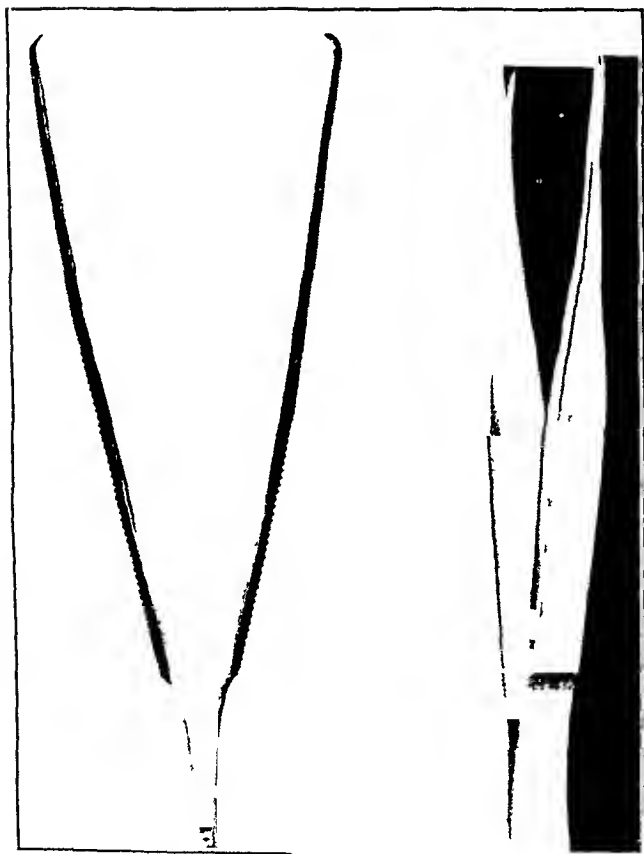


Fig 2—Globe fixation forceps

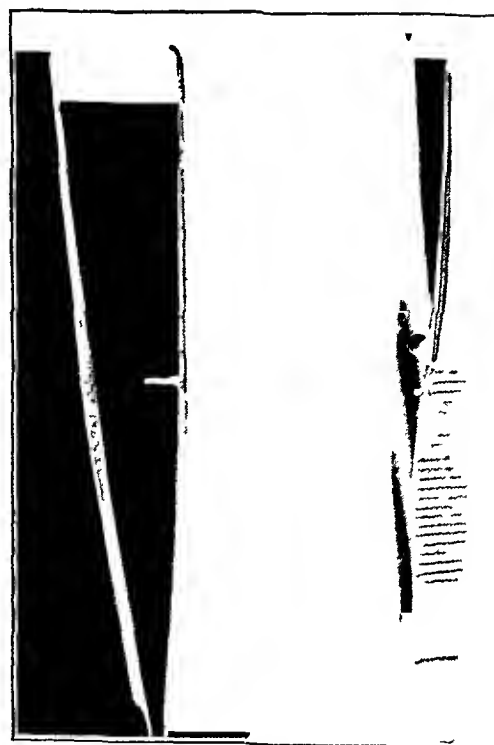


Fig 3—Corneoscleral suture forceps

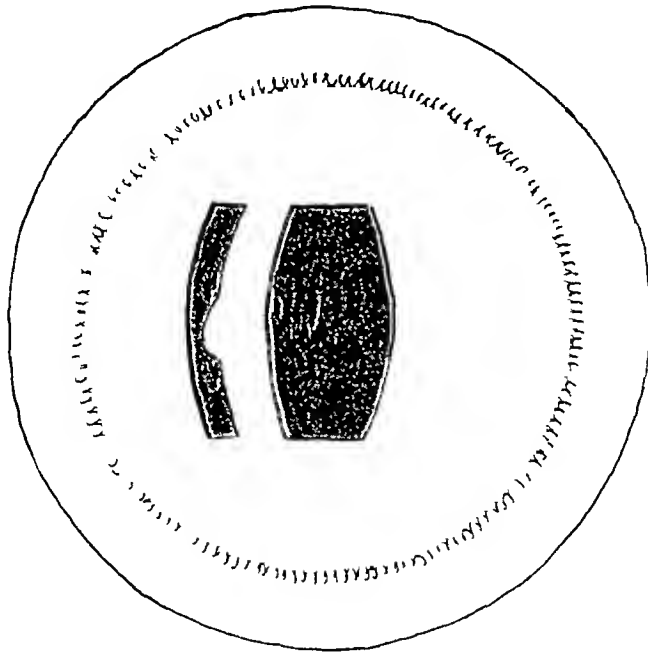
# KERATOCONUS POSTICUS CIRCUMSCRIPTUS

## Report of a Case

PHILIP B. GREENE, M.D., SPOKANE, WASH.

There have been 3 cases reported in the English literature<sup>1</sup> and, recently, 2 in the American literature<sup>2</sup> of a condition termed keratoconus posticus circumscriptus. The following case of a patient seen in 1940, which was written up at that time but not published, is of interest in that it may shed some light on the etiology of this minor, and apparently rare, abnormality.

Examination disclosed normal conjunctivas and lids. The pupils were round and equal and reacted to light and in accommodation. Focal illumination revealed a small, faint nebula in the left cornea. The right cornea was normal. Vision was 20/200 in each eye without correction. With a -2.50 D sphere, vision in the right eye was corrected to 20/20. Retinoscopic examination of the left eye showed a refractive error of +0.50 D sph  $\ominus$  +0.75 D cyl, axis 65, and correction gave 20/100 vision.



Optical section through the cornea and lens, showing the arrangement of the opacities in a direct line

C. E. D., a 52 year old, white business man, consulted me for a refraction on Oct 5, 1940. His only complaint was difficulty in reading for any length of time. He had worn glasses since childhood, and he volunteered the information that his left eye had never been as good as his right. His health had been excellent for many years. There was no unusual ocular condition in his ancestors. A son, in school, was myopic. No history of trauma was elicited.

1 (a) Butler, T. H. Keratoconus Posticus, Tr Ophth Soc U Kingdom **50** 551, 1930, (b) Two Rare Corneal Conditions, Brit J Ophth **16** 31, 1932, (c) Discussion of the Rarer Forms of Keratitis, Tr Ophth Soc U Kingdom **57** 32, 1937 (d) Stallard, in discussion on Butler<sup>1a</sup> (e) Ingram, H. V. Keratoconus Posticus, Tr Ophth Soc U Kingdom **56** 263, 1936

2 (a) Leopold, I. H. Keratoconus Posticus Circumscriptus, Arch Ophth **30** 732 (Dec.) 1943 (b) Wise, G. Keratoconus Posticus Circumscriptus, Am J Ophth **27** 1406, 1944

The interesting features of the left eye and the explanation of his poor vision were disclosed by the corneal microscope.

Situated in the middle of the cornea horizontally, but lying somewhat nasally, was the nebula previously mentioned. This was roughly about 3 mm in diameter and consisted of responsive changes in the substantia propria. Seen in thin optical section and in "block," the cornea was perfectly regular on the anterior surface, but posteriorly it described a sharp anterior curve, with a resultant total thickness of the cornea at this point of about one-third that of the adjacent clear areas. The rest of the cornea was normal. The substantia propria in this area was fairly clear, most of the opacity lying roughly in a ring around it, but the borders of the nebula were not sharp. There was no ectasia of this local thin section.

There was a small anterior subcapsular opacity, about 1 mm in circumference, slightly nasal to the center of the lens. Under this was a clear area of anterior cortex and adult nucleus. A dense round, white

opacity, somewhat larger, was situated on the face, or in the superficial layers, of the fetal nucleus. The posterior Y suture could be plainly made out, and on the posterior capsule, nasally, could be seen the former site of the hyaloid vessels. Scattered throughout both lenses were fine, punctate, grayish white dots, which were not refractile. The lens of the right eye showed no other opacities except changes in the posterior capsule marking the site of the hyaloid artery. As shown in the diagram, the opacities in the cornea and the lens were in a direct line and gave the impression that such a lesion could have been produced by piercing the cornea and the lens with a needle.

## COMMENT

The origin of this undoubtedly congenital condition must remain speculative. The mechanism could be explained by intrauterine inflammation or by an aberration in development.

The time element is fairly definite, as the deepest suture of the lens, the anterior (and the posterior) Y, is formed between the third and the seventh month approximately (Mann). Formation of an adhesion, the result of intrauterine inflammation, between the cornea and the lens at this time, when the anterior chamber is very shallow, might conceivably result in such a condition. This has been said by some authors to occur in cases of anterior lenticonus and of anterior capsular cataract, but this perhaps is not a true explanation, maldevelopment of the anterior zonule explaining the former and weakness in the anterior capsule, possibly a result of the lenticonus, accounting for the latter.

Delayed separation of the lens vesicle from the surface epithelium<sup>3</sup> or, more probably, from the cornea occurring at a later date must be considered. Collins and Parsons<sup>4</sup> described a case of such a nature in a chick, in which the lens vesicle had closed but remained in contact with the cornea. Descemet's membrane had failed to form, and the lens, perfectly developed, remained adherent to the substantia propria. Assuming a similar occurrence in this case, it is conceivable that the adhesion to the cornea ruptured,

freeing the lens, but too late to let the normal formation of substantia propria, endothelium and Descemet's membrane from the surrounding mesoblast proceed.

A somewhat similar fetal nuclear opacity, resulting from the adhesion to the lesser circle of the iris, has been described (Conway and Thomson<sup>5</sup>). The adhesion persisted and extended through clear zones of the lens to the iris.

Most congenital opacities of the cornea are ascribed to intrauterine inflammation, and they were termed internal ulcers by von Hippel<sup>6</sup>. Associated inflammation of the anterior uveal tract was described. Absence of Descemet's membrane in the affected area of the cornea is the most characteristic feature. However, Peters<sup>6</sup> suggested as the cause an ectodermal failure or a delay in separation of the lens vesicle, and Collins and Mayou<sup>6</sup> suggested a failure in mesodermal development, resulting in a hiatus in Descemet's membrane. Corneal opacities may be secondary to mechanical rupture of Descemet's membrane in cases of buphthalmos.

As pointed out by Leopold,<sup>2a</sup> Stallard<sup>1a</sup> described the first case of keratoconus posticus circumscriptus, and Butler and Ingram each reported a case, to which have since been added a case by Leopold<sup>2a</sup> and 1 by Wise. This condition is not the same as that which Butler described also under the term keratoconus posticus, the latter is a regular, geometrically precise increase in the curvature of the entire posterior surface of the cornea.

## CONCLUSION

A sixth case of keratoconus posticus circumscriptus is described. It is possible that this condition represents a delayed separation of the lens from the cornea and is an aberration in development, although intrauterine inflammation may be considered a possible cause.

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<sup>3</sup> Hess, in Graefe, A., and Saemisch, T. *Handbuch der gesamten Augenheilkunde*, Leipzig, W. Engelmann, 1911, vol. 11, pt. 9.

<sup>4</sup> Collins, E. T., and Parsons, J. H. *Tr. Ophth. Soc. U. Kingdom* **23**: 244, 1903.

<sup>5</sup> Conway, J. A., and Thomson, J. M. *Rare Form of Developmental Cataract*, *Brit. J. Ophth.* **13**: 402, 1929.

<sup>6</sup> Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1282.

# Ophthalmologic Reviews

EDITED BY DR FRANCIS HEED ADLER

## BLEPHAROPTOSIS

RAYNOLD N BERKE, M D

HACKENSACK, N J

- I Definition Ptosis may be divided into two types
  - 1 Pseudoptosis
  - 2 True ptosis
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    - B Congenital
    - C Hereditary
- II Etiology
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- V Preoperative Study of Ptosis Should Include
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  - 5 Horizontal length of palpebral fissure
  - 6 Position of lid fold of each upper lid
  - 7 Vertical width of upper tarsus
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  - 9 Sensibility of cornea
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  - 3 Nerve pathways
- VII Physiology of Upper Lid
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- VIII Surgical Treatment of Ptosis
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      - a Surgical variations
        - (a) Suture material from lid to the frontalis muscle
        - (b) Skin flaps from lid to frontalis muscle
        - (c) Strips of orbicularis muscle from lid to frontalis muscle
        - (d) Levator tendon from lid to frontalis muscle
        - (e) Strips of fascia lata from lid to frontalis muscle
        - (f) Flaps of frontalis muscle from brow to upper lid
      - b Comment
        - (a) Indications and contraindications
        - (b) Advantages and disadvantages
        - (c) Results of frontalis type of operation
        - (d) Reasons for failure
          - (a') Stretching of scar bands
          - (b') Weakness of frontalis muscle
    - B Utilization of superior rectus muscle
      - a Surgical variations
        - (a) Strip of superior rectus muscle to tarsus
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        - (c) Upper tarsus to superior rectus muscle
        - (d) Fascia lata from superior rectus muscle to tarsus
        - (e) Strips of orbicularis from tarsus to superior rectus muscle

## b Comment

- (a) Indications and contraindications
- (b) Advantages and disadvantages
- (c) Results of superior rectus type of operation
- (d) Reasons for failure
  - (a') Pulling away of muscle strip
  - (b') Weakness of superior rectus muscle

## C Utilization of levator palpebrae muscle

## a Surgical variations

- (a) Shortening of levator muscle through conjunctiva
- (b) Shortening of levator muscle through skin
- (c) Excision of part of lid
  - (a') Resection of tarsus
  - (b') Resection of orbicularis muscle
  - (c') Resection of orbicularis muscle and skin
  - (d') Resection of part of entire thickness of lid

## b Comment

- (a) Indications and contraindications
- (b) Advantages and disadvantages
- (c) Results of shortening levator
- (d) Reasons for failure
  - (a') Weak levator muscle
  - (b') Pulling out of sutures
  - (c') Resection of Muller's muscle instead of resection of levator muscle or its aponeurosis
  - (d') Insufficient resection

## IX Criteria for Perfect Operation for Ptosis

## X Summary

## XI Conclusion

## DEFINITION

Blepharoptosis is an abnormal drooping of the upper lid and may be divided into pseudoptosis and true ptosis. The former may be caused by an abnormal widening of the palpebral fissure on one side, thus producing an apparent ptosis on the other, or it may be due to disease or increased weight of the lid on the side of the ptosis, such as occurs with edema, elephantiasis, relaxed skin, prolapsed orbital fat, blepharochalasis, trachoma, tumors, endophthalmos, spasm of the orbicularis muscle and neurofibromatosis. True ptosis results from inadequate lifting power of the levator palpebrae muscle and is caused by an abnormality of the levator muscle or of its nerve supply. It may be congenital, acquired or hereditary in origin, unilateral or bilateral, partial or complete.

## ETIOLOGY OF PTOSIS

## ACQUIRED PTOSIS

Acquired ptosis is usually due to a lesion of the nervous system, to trauma or to disease of the upper lid. According to Wilbrand and

Saenger,<sup>1</sup> the chief causes of acquired ptosis are

1 Acute or subacute diseases, such as diphtheria, influenza, measles, erysipelas, epidemic cerebral meningitis, typhus, pneumonia, acute rheumatism and septicemia

2 Intoxications, such as occur from the coal tar derivatives, lead poisoning and botulism

3 Syphilis of the upper lid, the orbit, the roots of the third nerve, the nucleus of the third nerve, the supranuclear centers or the cortical centers

4 Lesions of the brain substance, such as hemorrhage, softening of the brain, abscess formation, meningitis, sinus thrombosis and brain tumor

5 Other causes, such as myasthenia gravis, trauma, multiple neuritis, Landry's paralysis, polyneuritis, diseases of the orbit or the nasal sinuses, Horner's syndrome, late acquired hereditary ptosis and hysteria

Acquired ptosis does not become a surgical problem until one is certain that other means of treatment will not effect a cure, and then only if curing the ptosis does not result in diplopia, corneal exposure or ulceration

## CONGENITAL PTOSIS

The cause of congenital ptosis is either a developmental defect of the levator muscle or a lesion of the central nervous system. Because facts to prove either theory are few and inconclusive, there is no unanimity of opinion on this subject, some authors contending that the cause is primarily nervous and others that it is primarily muscular. Evidence to support either theory comes from biopsies, operative observations and postmortem examinations of patients with congenital ptosis. Embryology and comparative anatomy also help to explain the origin of congenital ptosis.

*Anatomic and Histologic Studies on Congenital Ptosis*—In 1900 Wilbrand and Saenger,<sup>1</sup> in their monumental work, reviewed the literature on congenital ptosis up to that time. They were able to find the report of only 1 case in which the entire orbital contents had been examined post mortem. This was Heuck's<sup>2</sup> report on a family in which congenital ptosis affected the mother, aged 53, two sons, aged 18 and 16, and a daughter, aged 12. All had had complete ptosis since birth and showed defective ocular motility in

1 Wilbrand, H., and Saenger, A. *Die Neurologie des Auges*, Wiesbaden, J. F. Bergmann, 1900, vol. 1, p. 85

2 Heuck, G. Ueber angeborenen vererbten Beweglichkeits-Defect der Augen, *Klin. Monatsbl. f. Augenh.* 17: 253, 1879



all directions, especially in upward gaze. The 18 year old youth died, and both orbits were removed post mortem for examination. In the right orbit a poorly developed levator muscle, only 2 mm wide, was found. In the left orbit no trace of the levator was detectable, even though special search was made for it. Examination of the other extraocular muscles showed that the superior rectus muscles were very thin and almost membranous and that the other rectus muscles were abnormally inserted into the globe. He made no study of the third nerve or of its nucleus. In 1895 Bach<sup>3</sup> reported a case of a girl aged 18 who had congenital ptosis, epicanthus and limitation of extraocular motility. After death large pieces of the muscles of the eye were removed. Microscopic study showed marked atrophy and poor development of the levator, as well as atrophy of the superior rectus. In 1895 Ahlstrom<sup>4</sup> described a case of complete congenital ptosis in which only a few tendon fibers were demonstrable in the right upper lid and there was no trace of a levator tendon in the left upper lid. Other anatomic defects of the extraocular muscles associated with congenital ptosis are<sup>1</sup> bifurcation of the internal rectus, failure of separation of the muscles, abnormal insertions, connective tissue strands in place of muscles and complete failure of the muscles.

A few authors have demonstrated changes in the third nerve, or in the nucleus of the third nerve, but in most of the cases ptosis has been associated with hydrocephalus or other disease of the central nervous system. At operation Bach<sup>3</sup> observed a case of congenital ptosis in which the levator tendon was demonstrated to be normally inserted and of normal length and width. He concluded, without examining the brain or the entire orbit, that here there must have been a defect of nerve conduction or an aplasia of the nuclear region of the third nerve. Siemerling<sup>5</sup> examined the brain and the orbits of a patient with mild unilateral congenital ptosis and inactive pupils. Autopsy showed leptomeningitis, a subdural hemorrhage and purulent bronchitis. Histologic examination of the brain and orbits showed mild degeneration of the levator muscle fibers on the side of the ptosis and bilateral degener-

ation of certain portions of the nucleus of the third nerve. He speculated that the cause of the ptosis in his case was a defective development of the nucleus of the third nerve. Wilbrand and Saenger<sup>1</sup> described degenerative changes in the nucleus of the third nerve of a man with bilateral congenital ptosis who died of tuberculosis at 47 years of age. They did not study the orbits or the levator muscles.

Several cases of congenital ptosis, associated with limitation of extraocular motility, are reported in the literature as instances of ophthalmoplegia externa. In 1924 Posey<sup>6</sup> reviewed the literature on anomalies of the extraocular muscles and added observations of his own. In 1927 Macklin<sup>7</sup> made some additional reports. Calhoun,<sup>8</sup> Stephenson,<sup>9</sup> Lawford,<sup>10</sup> Harman,<sup>11</sup> McCubbin,<sup>12</sup> de Schweinitz<sup>13</sup> and others<sup>14</sup> have contributed to this subject.

A review of the literature on the anatomic observations in cases of congenital ptosis shows that when such studies have been carried out some defect of the levator muscle has always been found. In those few cases in which defects have been noted in the third nerve or its nucleus, these defects could be explained on the basis of hydrocephalus, the presence of disease of the brain or an ascending degeneration of the third

6 Posey, W. C. Concerning Some Gross Structural Anomalies of the Muscles of the Eye and Its Adnexa, *Arch Ophth* **53** 344-354 (July) 1924.

7 Macklin, M. T. Hereditary Abnormalities of the Eye, *Canad M A J* **16** 1340-1342 (Nov.) 1926, **17** 55-60 (Jan.), 327 (March), 421 (April) 1927.

8 Calhoun, F. P. Chronic Progressive Ophthalmoplegia Externa, *South M J* **20** 923-925 (Dec) 1927.

9 Stephenson, S. A Case of Incomplete Congenital Ophthalmoplegia Externa, *Ophthalmoscope* **6** 678-685, 1908.

10 Lawford, J. B. Congenital and Hereditary Defects of Ocular Movements, *Ophth Rev* **6** 363, 1887, Congenital Hereditary Defects of Ocular Movements, *Tr Ophth Soc U Kingdom* **8** 262-274, 1888.

11 Harman, N. B. Absence of Internal and External Recti Muscles, *Tr Ophth Soc U Kingdom* **25** 281-286, 1904-1905.

12 McCubbin, J. B. A Case of Congenital Immotility, Extrinsic and Intrinsic, *Am J Ophth* **28** 69-73, 1911.

13 de Schweinitz, G. E. Complete Bilateral Congenital Ophthalmoplegia and Double Ptosis. Bilateral Cerebral Cortical Atrophy of Frontal and Parietal Regions (Encephalograms), Clinical Communication, *Arch Ophth* **5** 15-28 (Jan) 1931.

14 Steinheim. Blepharoptosis congenita und Defect der Musculi recti superiores, *Klin Monatsbl f Augenh* **15** 99-102, 1877. Pflüger. Strabismus congenitus (2 Falle), *ibid* **14** 157, 1876. Natale, A. Ptosis congenita y anomalías musculares, *Rev de especialid* **3** 908-917 (Dec) 1928.

3 Bach, L. Anatomischer Befund eines doppel-seitigen angeborenen Kryptophthalmos beim Kaninchen, *Arch f Augenh* **32** 16-32, 1895-1896.

4 Ahlstrom, G. Doppelseitige kongenitale Ptosis und Unbeweglichkeit der Bulbi, *Beitr z Augenh* **11** 523, 1895.

5 Siemerling, E. Anatomischer Befund bei ein-seitiger congenitaler Ptosis, *Arch f Psychiat* **23** 764-774, 1891-1892.

nerve Von Gudden,<sup>15</sup> Brouwer,<sup>16</sup> Chace<sup>17</sup> and others<sup>18</sup> have shown that removal of the eye or one of the extraocular muscles in very young animals results in degenerative changes in the nuclei concerned. Therefore, one would expect to find secondary changes in the nucleus of the third nerve in all cases of congenital ptosis. Also, the fact that the internal muscles of the eye are not affected in cases of ptosis is a strong point against the theory of the nervous origin of ptosis. Rodin and Barkan<sup>19</sup> were unable to find more than 1 undisputed case of hereditary congenital total ophthalmoplegia in the literature. Certainly, if congenital ptosis were due primarily to a lesion of the nucleus of the third nerve, the accommodation and pupillary reflexes should be affected more often. Furthermore, abnormal insertions, bifurcation and incomplete separation of the muscles and other anatomic defects associated with ptosis cannot be explained satisfactorily by the theory of a nervous origin.

*Comparative Anatomy and Embryology of the Levator Palpebrae Muscle*—Comparative anatomy shows that the earliest extraocular muscles in the lowest vertebrates appeared simultaneously with the eye and have remained essentially unchanged throughout the entire vertebrate series. Indeed, except for the absence of the levator in the lower vertebrates, the number and nerve relationships of the extraocular muscles are essentially the same in man as in the dogfish.<sup>20</sup> The levator muscle appears first in the mammals and is the most recently acquired of the extraocular muscles.<sup>21</sup> The fact that recently acquired struc-

tures are more vulnerable to abnormal development may explain why the levator is often defectively developed in man.

Embryonically the levator muscle does not appear until comparatively late. The first trace of the extraocular muscles in man can be seen at the 7 mm stage. During the 20 mm stage the four rectus muscles and the two oblique muscles can be recognized.<sup>22</sup> The levator muscle develops later from the medial side of the superior rectus in the third month but does not reach its final position until the 75 mm stage, or the fourth month. This pattern of development is of clinical interest because it helps to explain the cause of congenital ptosis. For example, if this developmental process should be hindered before the 20 mm stage, any or all of the extraocular muscles will be defective. If development after the 20 mm and before the 75 mm stage should be hindered, the levator will be defective or absent. If the superior rectus fails to develop, the levator is always absent, although the reverse does not occur. This explains the frequent association of ptosis with weakness of the superior rectus and bears out the clinical observation that "no case of defective upward movement of the eye with perfect movement of the lid is known."<sup>23</sup>

The embryonic origin of Muller's<sup>24</sup> muscle of the upper lid is unknown. Ida Mann does not discuss this subject, nor do any of the standard textbooks on embryology. However, from comparative anatomy one learns that the anlage of Muller's muscle existed long before the levator appeared phylogenetically. Groyer<sup>25</sup> showed that in the water mammals this muscle is made up of striated muscle fibers but that in land mammals it consists of smooth muscle fibers. In the seal

15 von Gudden, cited by Howe, L. *The Muscles of the Eye*, New York, G. P. Putnam's Sons, 1907, vol 1, p. 96.

16 Brouwer, B. Klinisch-anatomische Untersuchung über den Oculomotoriuskern, *Ztschr f d ges Neurol u Psychiat* **40** 152-189, 1918.

17 Chace, R. R. Structural Changes in External Geniculate Body of Rat Following Removal of Eyes, *Arch Ophth* **30** 75-86 (July) 1943.

18 Hamburger, V. The Effects of Wing Bud Extirpation on the Development of the Cerebral Nervous System in Chick Embryos, *J Exper Zool* **68** 449-494 (Aug) 1935. Bernheimer, S. Die Reflexbahn der Pupillarreaction, *Arch f Ophth* **47** 1, 1899, cited by Stevens, G. T. *Motor Apparatus of the Eyes*, Philadelphia, F. A. Davis Company, 1906.

19 Rodin, F. H., and Barkan, H. Hereditary Congenital Ptosis. Report of Pedigree and Review of Literature, *Am J Ophth* **18** 213-225 (March) 1935.

20 Neal, H. V. The History of the Eye Muscles, *J Morphol* **30** 433-453, 1918.

21 (a) Comparative Ophthalmology, in Wood, C. A. *American Encyclopedia and Dictionary of Ophthalmology*, Chicago, Cleveland Press 1914, vol 4, p. 2621. (b) Walls, G. L. The Vertebrate Eye and Its Adaptive Radiation, Bulletin 19, Cranbrook Institute of Science,

1942. (c) Waardenburg, P. J. Die Zurückführung einer Reihe erblich-angeborener familiärer Augenmissbildungen auf eine Fixation normaler fetaler Verhältnisse, *Arch f Ophth* **124** 221-299, 1930. (d) Collins, E. T. Changes in the Visual Organs Correlated with the Adoption of Arboreal Life and with the Assumption of Erect Posture, *Tr Ophth Soc U Kingdom* **41** 10-90, 1922.

22 Mann, I. *The Development of the Human Eye*, London, Cambridge University Press, 1928.

23 Mann, I. *Developmental Abnormalities of the Eye*, London, Cambridge University Press, 1937.

24 Muller, A. Ueber glatte Muskeln an den Augenlidern des Menschen und der Säugethiere, *Verhandl d phys-med Gesellsch in Würzburg* **9** 244, 1859.

25 Groyer, F. Vergleichende Anatomie des Musculus orbitalis und der Musculi palpebrales, *Sitzungsber d k Akad d Wissensch Math-naturw Cl* **112** 51-100, 1903. Zur Anatomie des Musc palpebral sup des Menschen, *Ztschr f Augenh* **14** 365, 1905. Ueber der Zusammenhang der Musculi tarsales mit den geraden Augenmuskeln beim Menschen und Säugetieren, *Internat Monatschr f Anat u Physiol* **23** 210-226, 1906.

and the dolphin, neither of which have a levator muscle, the superior rectus branches as it approaches the eyeball, one branch going to the globe and the other to the upper lid. In all land mammals Muller's muscle has become separated from the superior rectus and is a part of the levator. Groyer stated the belief that both the levator and Muller's muscle develop from the superior rectus but that Muller's muscle is older phylogenetically. This may explain why Muller's muscle has never been described as absent in cases of ptosis, probably because phylogenetically older organs are less vulnerable to atavism or to abnormal development than are newly acquired ones.

The treatment of congenital ptosis is primarily surgical and will be discussed with the various operations devised to remedy this condition.

#### HEREDITARY PTOSIS

Hereditary ptosis may manifest itself at birth (congenital type) or later in life (adult and juvenile types). The congenital variety is most likely due to a developmental defect of the levator muscle. Usually only one member of a family is affected, but sometimes congenital ptosis is familial and then can be transmitted either as a dominant or as a recessive characteristic. A number of excellent pedigrees on familial ptosis have been reported. In 1919 Briggs<sup>26</sup> presented a family tree in which hereditary congenital ptosis affected 64 members, distributed over 6 generations, both males and females being affected, according to the mendelian rule of dominance. In all but 1 of his cases the superior rectus was normal. Usher<sup>27</sup> published a pedigree in which bilateral ptosis associated with epicanthus affected 18 members, all the affected persons being in continuous line of descent from 1 affected male. The author pointed out that congenital ptosis without epicanthus is common, ptosis with epicanthus is less common and epicanthus without ptosis is rare. Ross<sup>28</sup> and McIlroy<sup>29</sup> also reported pedigrees showing association of ptosis with epicanthus. Rodin and Baikan<sup>30</sup> recorded

bilateral ptosis with incomplete external ophthalmoplegia in a mother and 2 daughters. Rodin<sup>30</sup> later reported the pedigree of 4 generations in which hereditary congenital ptosis affected only one eye and the pedigree of 1 generation in which bilateral congenital ptosis was associated with epicanthus. Ptosis associated with blepharophimosis, affecting 21 out of 38 persons in 5 generations, was noted by Dimitry.<sup>31</sup> Bradburne<sup>32</sup> reported on a family in which bilateral ptosis associated with hereditary ophthalmoplegia affected 5 generations. De Schweinitz<sup>33</sup> described in detail the encephalograms of a patient with congenital ptosis and external ophthalmoplegia. Tatar and von Pap<sup>33</sup> reported cases of ptosis associated with mental weakness. Waardenburg<sup>21c</sup> describes defects of the inner canthus in patients with ptosis. A case of jaw-winking associated with ptosis was reported by Sinclair.<sup>34</sup> A rare type of paradoxical ptosis was described by Yanes.<sup>35</sup>

The noncongenital, or late developing, type of hereditary ptosis is rare. It was first described by Fuchs<sup>36</sup> in patients between 30 and 60 years of age. Collins<sup>37</sup> described a case of this type which he attributed to abiotrophy—a sort of hereditary lack of vital force affecting the levator muscle. Forsberg<sup>38</sup> cited the pedigrees of 67 persons, of whom 6 males and 6 females had the onset of ptosis between the ages of 5 and 20 years of age.

#### INCIDENCE OF PTOSIS

No figures are available for the incidence of ptosis in the general population, but hospital reports show that operations for ptosis comprise less than 1 per cent of all surgical procedures on the eye. Of 4,726 operations on the eye done

26 Briggs, H. H. Hereditary Congenital Ptosis with Report of Sixty-Four Cases Conforming to the Mendelian Rule of Dominance, *Am J Ophth* **2** 408-417 (June) 1919.

27 Usher, C. H. A Pedigree of Epicanthus and Ptosis, *Ann Eugenics* **1** 129-138, 1925.

28 Ross, N. Congenital Epicanthus and Ptosis Transmitted Through Four Generations, *Brit M J* **1** 378-379 (Feb 27) 1932.

29 McIlroy, J. H. Hereditary Ptosis with Epicanthus. Case with Pedigree Extending over Four Generations, *Proc Roy Soc Med (Sect Ophth)* **23** 17-20 (Jan) 1930.

30 Rodin, F. H. Pedigree of Four Generations of Hereditary Congenital Ptosis Affecting Only One Eye and Pedigree of One Generation of Congenital Ptosis with Epicanthus, *Am J Ophth* **19** 597-599 (July) 1936.

31 Dimitry, T. J. Hereditary Ptosis, *Am J Ophth* **4** 655-658 (Sept) 1921.

32 Bradburne, A. A. Hereditary Ophthalmoplegia in Five Generations, *Tr Ophth Soc U Kingdom* **32** 142-153, 1911-1912.

33 Tatar, J., and von Pap, V. Erbliche Ptosis und Schwachsinn, *Arch f Ophth* **142** 627-633, 1941.

34 Sinclair, W. W. Abnormal Associated Movements of the Eyelids, *Ophth Rev* **14** 307-319, 1895.

35 Yanes, T. R. Paradoxical Monocular Ptosis, *Arch Ophth* **23** 1169-1172 (June) 1940.

36 Fuchs, E. Ueber isolierte doppelseitige Ptosis, *Arch f Ophth* **36** (pt 1) 234-259, 1890.

37 Collins, E. T. Hereditary Ocular Degenerations—Ophthalmic Abiotrophies, *Internat Cong Ophth* **1** 103-143, 1922.

38 Forsberg, C. W. Hereditary Ptosis, *Journal-Lancet* **52** 378-380 (June) 1932.

at Wills Hospital<sup>39</sup> in 1941, 32, or 0.69 per cent,<sup>40</sup> were for ptosis. The incidence of operations for ptosis ranked twenty-seventh in the list of operative procedures performed. Of 19,146 operations on the eye done at the New York Eye and Ear Infirmary<sup>41</sup> for the seven year period from 1936 to 1942 inclusive, 168, or 0.88 per cent were for ptosis. The average number of operations for ptosis per year at this institution was 24. At the Manhattan Eye, Ear and Throat Hospital,<sup>42</sup> 2,971 operations on the eye were done in 1941, 17, or 0.57 per cent, of which were for ptosis.<sup>40</sup> In 1932 Moorfields Hospital, London,<sup>43</sup> had 3,276 "in patients" of whom 23, or 0.97 per cent, had operations, for ptosis. The ratio of congenital to acquired ptosis is about 3 to 1. In 1932 Moorfields Hospital did 23 operations for ptosis, 16 of which were for the congenital and 7 for the acquired type. In 1941 the New York Eye and Ear Infirmary did 26 operations for ptosis, 20 of which were for congenital and 6 for acquired ptosis.

The kind of operation for ptosis done at each hospital was generally not listed in the annual reports, but when the type was listed, it seemed to vary according to the locality of the hospital. At Moorfields Hospital, the Lexer operation (strips of fascia lata to the frontalis muscle) was generally done. Of the 17 cases in which operation was performed for ptosis at the Manhattan Eye, Ear and Throat Hospital, the Blaskovics procedure was done in 8, the Gillet de Grandmont operation in 3, the Eversbusch in 2, the Wheeler operation in 2, the Steatfield-Snellen operation in 1 and the Young operation in 1. At the latter institution, therefore, resection or shortening of the levator muscle was the procedure of choice.

#### CLINICAL ANOMALIES ASSOCIATED WITH CONGENITAL PTOSIS

A review of the literature on congenital ptosis shows that the following clinical anomalies may be associated with ptosis:

##### A Abnormal extraocular motility

- 1 Weakness of the superior rectus muscle
- 2 Weakness of the superior rectus and the inferior oblique muscle

<sup>39</sup> Report from the Wills Hospital, Philadelphia, 1941.

<sup>40</sup> This percentage is low because minor operations, such as those for chalazion, were included in the statistics.

<sup>41</sup> Annual Report of the New York Eye and Ear Infirmary, New York, 1936-1939, 1940-1942.

<sup>42</sup> Report of the Manhattan Eye, Ear and Throat Hospital, New York, 1941.

<sup>43</sup> Report of the Moorfields Hospital, London, 1932.

- 3 Esotropia or exotropia
- 4 Weakness or fibrosis of the external rectus muscle (retraction syndrome of Duane)
- 5 More or less complete external ophthalmoplegia, with absence, bifurcation or abnormal insertion of the extraocular muscles

##### B Abnormal development of the lids

###### 1 Epicanthus

- (a) Superciliary type—a fold of skin extending from the brow to the lower lid
- (b) Palpebral type—a fold of skin extending from the upper lid above the tarsus to the lower lid
- (c) Tarsal type—a fold of skin extending from the tarsal portion of the upper lid to the lower lid

###### 2 Blepharophimosis—an abnormally short fissure horizontally

- 3 Abnormal inner canthus, e. g., an abnormally long inner canthal ligament, with defective development of the canuncle and the semilunar fold

##### C Abnormal innervation of the levator muscle, producing jaw-winking (Marcus Gunn phenomenon)

##### D Other abnormal developmental defects such as extra toes and fingers and feeble-mindedness

#### PREOPERATIVE STUDY OF PTOSIS

Before every operation to correct ptosis the following data should be determined:

- 1 The amount of ptosis in the eyes up, in the eyes straight ahead and in the eyes down position
- 2 The amount of the function of the levator present, if any
- 3 The extraocular motility of each eye, especially that of the superior rectus muscle
- 4 The length of the palpebral fissures horizontally
- 5 The position of the upper lid fold of each eye
- 6 The vertical width of the tarsus
- 7 The effect on the ptosis of instillation of drops of cocaine
- 8 The vision of the two eyes and the presence of fusion, diplopia or amblyopia
- 9 The sensibility of the cornea

There is no entirely satisfactory way to measure ptosis. Dianoux and associates<sup>44</sup> used a perimeter, asking the patient to read a card as it was moved upward along the arc of the perimeter. The place where the lid covered the pupil and reading became impossible was noted and recorded in degrees as a measure of the ptosis present. This method has several disadvantages. It cannot be used with small children, with amblyopic eyes, or with paralysis of the superior rectus. Bulky equipment is necessary, and, what is more important, it is difficult to transpose the readings into figures which have meaning to the surgeon at the time of operation.

A second method consists in measuring the vertical width of the palpebral fissure of each eye in three directions of gaze, namely, with eyes looking up, with eyes looking straight ahead and with eyes looking down. This method has one disadvantage, namely, the movement of the upper lid is measured from a nonstationary object, the lower lid. It is well known that the lower lid moves upward when one is looking up and moves down when one is looking down. In cases of complete ptosis, in which there is no movement of the upper lid, the vertical width of the palpebral fissure may be 1 mm or less with eyes looking up, 2 mm with eyes straight ahead and as much as 5 or 6 mm with eyes looking down. Measurements of this kind give an erroneous impression of the function of the levator because any variation in the width of the palpebral fissure is due solely to the rise and fall of the lower lid, and not to elevation of the upper lid. Furthermore, these measurements of ptosis are of little help to the surgeon at the time of operation in determining the amount of resection of the levator to be done because the base line, from which the measurements are taken, (the margin of the lower lid) is a nonstationary one.

A third method of measuring ptosis is to use the orbital rim at its highest point as the base from which to measure movements of the upper lid. This can be done with a compass, a millimeter rule, a Jameson rule or some similar instrument for measuring. While the patient is looking down, the examiner's thumb is placed above the patient's brow to steady one end of the rule, which is placed against or at the level of the superior orbital rim. The distance from the

orbital rim to the margin of the upper lid is noted. The patient is then asked to look straight ahead, and the amount of elevation of the lid is noted in this position, as well as when he is looking up. This method measures directly the amount of ptosis and the elevation of the upper lid and, at the same time, prevents the frontalis muscle from affecting the measurements of ptosis. If the upper lid does not move upward when the eyes are looking up, complete ptosis is obviously present. With this method the surgeon can determine before operation the amount of correction needed and at the time of operation the amount of correction secured.

To the ophthalmic surgeon it is of the utmost importance to determine if possible the anatomic condition of the levator muscle before operation, especially if a resection of this muscle is contemplated. If the levator is entirely absent, it is utterly folly to attempt resection of something which does not exist. The surgeon has at his disposal three methods of determining the functional state of the levator muscle. First, if the lid is elevated, the fissure widened or the upper lid fold deepened in upward gaze while the frontalis is kept from acting, it is proof of action of the levator. Second, if the superior rectus is weak, the levator is often poorly developed or weak. Third, if the fissure becomes wider after instillation of a few drops of cocaine, the levator is presumed to be present.<sup>45</sup>

45 Ptosis due to paralysis of the sympathetic nerve supply to Muller's muscle (Horner's syndrome) may produce 3 to 4 mm of ptosis and may be "cured" by the instillation of eye drops of cocaine (Lancaster, W B. *Operative Treatment of Ptosis*, Tr Am Acad Ophth 24 235-263, 1919). This "cure" has been attributed to the action of cocaine directly on the smooth muscle of the upper lid. Certain authors have suggested the use of this test to determine the presence or absence of the levator muscle in cases of congenital ptosis. Adler (*Clinical Physiology of the Eye*, New York, The Macmillan Company, 1933, pp 6-12) stated that cocaine has no effect in cases of congenital ptosis because the levator is absent and Muller's muscle has no fixed point from which to lift the lid. Briggs<sup>26</sup> reported that cocaine had no effect on the ptosis in his cases, and he assumed that this was due to the absence of the levator. Bradburne<sup>32</sup> reported on a pedigree in which congenital ptosis ran through 5 generations and affected 17 out of 37 members, in some cases there was no action of Muller's muscle, while in others "the action of Muller's muscle was plainly seen on attempting to open the eye." Apparently, the author did not use cocaine. Just how he determined that this muscle was present was not disclosed. Koster (*Ztschr f Augenh* 3 304-307, 1900, *Nederl tijdschr v geneesk* 35 417-419, 1899, ab-

44 Dianoux, Duverger, C, and Velter, E, cited by Sedan, J, in Bailliart, P, Coutela, C, Redslob, E, and Velter, E. *Traite d'ophtalmologie*, Paris, Masson & Cie, 1939, vol 7, p 1066.



In addition to a study of the behavior of the levator, special attention should be paid to the function of the extraocular muscles. Associated with ptosis often is a weakness of elevation of the globe, which contraindicates any operation for ptosis until the hypotropia can be remedied. Especially is this true of those operations which utilize the lifting power of the superior rectus to support the ptosed lid. If the patient cannot roll his cornea upward under cover of the upper lid during sleep, exposure keratitis and loss of the eye may result. Also, exotropia and esotropia, if associated with ptosis, can best be remedied before the ptosis is corrected.

The horizontal length of the palpebral fissure should be measured in all cases of ptosis to rule out the presence of blepharophimosis. If this condition is present, the fissures should be lengthened before the ptosis is corrected.

The position of the upper lid fold of each eye should be recorded preoperatively, so that the surgeon will know at operation where to place the lid fold of the ptosed lid. Care in details like these produces better cosmetic results. The vertical width of the tarsus should be recorded preoperatively, so that the surgeon can estimate how much tarsus may be safely removed without producing a postoperative notch of the margin of the lid. De Blaskovics<sup>46</sup> advocated removing all but 1.5 mm of the tarsus if necessary. Most authorities advocate leaving at least 3 mm of tarsus in the midline to support the normal arch of the margin of the upper lid. The vertical width of the tarsus influences the amount of correction

stracted, *Jahresb u d Leistung u Fortschr im Geb d Ophth*, 1899, p 556) studied the effect on the upper lid of instilling drops of cocaine in the eyes of patients with congenital ptosis. He stated that if widening occurs it is proof that the levator is present. He assumed that Muller's muscle was always present in cases of congenital ptosis and concluded that if cocaine failed to elevate the lid the levator was absent. Mahoney and Sheehan (*Experimental Ptosis in Primates*, *Arch Neurol & Psychiat* **35** 99-108 [Jan] 1936) showed that after they had produced ptosis in monkeys by resection of the third nerve and the superior cervical ganglion, elevation of the lid occurred in fright or after the injection of epinephrine. They explained this elevation by assuming that the smooth muscle in the upper lid contracted even though the third nerve, the sympathetic fibers and the levator muscle were paralyzed. The value of the cocaine test for determining the presence of the levator muscle in cases of congenital ptosis seems at present somewhat uncertain, from available information.

46 de Blaskovics, L. Treatment of Ptosis. Formation of a Fold in the Eyelid and Resection of the Levator and Tarsus, *Arch Ophth* **1** 672-680 (June) 1929.

achieved in all operations which employ the superior rectus to elevate the lid (especially the operations of Trainor, Young, Greeves and Jameson), as well as the operation of tarsal resection, with or without resection of the levator.

Obviously, every patient with ptosis should have tests for visual acuity, fusion, diplopia and amblyopia. If the patient has good vision with fusion before operation, it is important to employ an operation for ptosis which is least likely to disturb his binocular vision. If diplopia is present before operation when the ptosed lid is elevated, this should be corrected before the ptosis is remedied. If amblyopia is present, the danger of disturbing fusion or of producing diplopia postoperatively is negligible, because here the object of the operation is primarily cosmetic. The tactile sensibility of the cornea should be noted preoperatively, for if the cornea is anesthetic one can be almost certain that uncovering the cornea will result sooner or later in neuroparalytic keratitis, with possible loss of the eye.

#### ANATOMY OF THE UPPER LID AND THE LEVATOR MUSCLE

From a special study of the orbits of cadavers and a careful perusal of the available textbooks<sup>47</sup> on the anatomy of the upper lid, one will note that the lid is made up of seven layers of tissue. These layers may be described, briefly, as follows:

1. The skin is firmly adherent to the underlying tissues of the brow and extends from the brow to the margin of the lid. About 5 or 6 mm above the lashes the skin is thrown into a horizontal fold, called the upper lid fold, which marks the line of insertion of the terminal fibers of the levator aponeurosis. These fibers serve to keep the loose skin of the upper lid from prolapsing over the lashes. Elsewhere the skin is loosely attached to the underlying orbicularis muscle, except at the margin of the lid and at the internal and external canthal ligaments.

47 (a) Whitnall, S. E. *Anatomy of the Human Orbit*, ed 2, New York, Oxford University Press, 1932. (b) Eisler, P. *Die Anatomie des menschlichen Auges*, in Schieck, H., and Bruckner, A. *Kurzes Handbuch der Ophthalmologie*, Berlin, Julius Springer, 1930, vol 1, p 198. (c) Hesser, C. *Der Bindegewebsapparat und die glatte Muskulatur der Orbita beim Menschen in normalen Zustände*, *Anat Hefte* **49** 1-302, 1913. (d) Kronfeld, P. C., McHugh, G., and Polyak, S. L. *The Human Eye*, Rochester, N. Y., Bausch & Lomb Press, 1943. (e) Wolff, E. *Anatomy of the Eye and Orbit*, Philadelphia, P. Blakiston's Son & Co., 1936. (f) Hildreth, H. R. Insertions of Levator Palpebrae Muscles, *Am J Ophth* **24** 749-758 (July) 1941.



2 The orbicularis oculi muscle is fused with the corrugator supercilii muscle and the frontalis muscle at the brow. It extends downward from the brow to the margin of the lid, being loosely attached to the skin in front and to the septum orbitale and the tarsus behind. Medially it is attached to the nasal orbital margin and the internal canthal ligament and laterally to the bone of the temporal margin of the orbit and the external raphe. At the level of the upper lid fold the orbicularis is fused with some of the terminal fibers of the levator aponeurosis as these pass through the orbicularis to become attached to the skin.

3 The septum orbitale begins at the orbital margin from the junction of the periosteum of the frontal bone and the periorbita of the orbit. At this point it is thickest, and from here downward it becomes thinner, as it hugs the posterior surface of the orbicularis. As a matter of fact, it seems more accurate surgically to conceive of this structure as the posterior fascial sheath of the orbicularis than to think of it as a separate structure. At about the level of the upper border of the tarsus the septum orbitale fuses with the levator aponeurosis, thus forming a barrier to the prolapse of the orbital fat which is nearly always found at this junction. Anterior to the tarsus one finds a thin layer of loose connective tissue which occupies the same relationship to the orbicularis muscle as does the septum orbitale above the tarsus and which, for practical purposes, can be considered a prolongation of this membrane. Medially the septum orbitale is adherent to the nasal orbital margin and laterally to the temporal orbital margin.

4 The orbital fat is posterior to the septum orbitale. It takes on a comma shape in sagittal sections, being thick and rounded in front and thin and pointed behind, and fills the triangular space between the sheath of the levator, below, the roof of the orbit, above, and the septum orbitale, in front.

5 Below and behind this roll of fat is the levator aponeurosis, which arises from the terminal fibers of the levator muscle and extends forward and downward to the tissues of the upper lid. It lies between the septum orbitale, in front, and Muller's muscle, behind, and is divisible, for description, into a medial and a lateral horn. The medial horn is thin and fragile and is difficult to follow as it passes from the levator muscle over the sheath of the reflected tendon of the superior oblique muscle to the upper border of the medial canthal ligament. The lateral horn is more dense and

fibrous than the medial horn. It passes from the levator muscle to the upper border of the external canthal ligament and separates the lacrimal gland into two parts, so that the main part of the gland lies above the lateral horn and the accessory lobe behind it. The middle part of the levator tendon, flanked by the two horns, is the portion generally removed in resection of the levator muscle. It is about 10 to 12 mm long and extends from the anterior end of the levator muscle toward the upper border of the tarsus, where, according to some authors, it seems to end. Careful dissection with a magnifying loupe will show that at the upper border of the tarsus the aponeurosis divides into thousands of fine fibrillae, which become attached partly to the anterior surface of the tarsus but chiefly to the overlying orbicularis and skin, producing the upper lid fold.

6 Muller's muscle is about 15 to 20 mm wide and 10 or 12 mm long and extends from the terminal fibers of the levator to the upper border of the tarsus. It is loosely adherent to the aponeurosis, on one side, and to the conjunctiva, on the other. Muller's muscle is about 0.5 to 1 mm thick, is very delicate and is easily torn.

7 The conjunctiva is firmly adherent to the tarsus and loosely attached to Muller's muscle. The upper fornix is supported by the conjoined sheaths of the levator and the superior rectus muscles, i. e., by the so-called suspensory ligament of the upper fornix. Muller's muscle is so delicate and so thin that when the conjunctiva is reflected upward, the muscle is usually reflected also, unless minute care is taken to separate the two structures.

The levator muscle is about 50 mm long, including its insertional attachments, and originates from the annulus of Zinn, at the apex of the orbit, directly above the origin of the superior rectus muscle. The under surface of the levator is in contact with the superior rectus all along its course. The fascial sheaths of these two muscles blend and become thicker as the globe is approached. This intimate association of the sheaths of the superior rectus and the levator may account for the occurrence of some elevation of the lid in upward rotation of the globe when the levator is completely paralyzed.

#### NERVE SUPPLY OF THE LEVATOR MUSCLE

As the third nerve enters the orbit through the superior orbital fissure and the annulus of Zinn, it branches into an upper and a lower division. The upper division supplies the superior rectus and the levator only. The inferior divi-

sion, besides supplying the internal rectus, the inferior rectus and the internal muscle of the eye, innervates the inferior oblique, which, together with the superior rectus, elevates the globe. The location of the higher centers, which control the synchronized up and down movements of the lid with the globe, have been definitely located in the vicinity of the angular gyrus of the frontal cortex.<sup>48</sup> The orbicularis, the antagonist of the levator, is supplied by the seventh cranial nerve. The higher centers controlling the reciprocal action of the orbicularis and the elevator must also be in the vicinity of the angular gyrus.

### PHYSIOLOGY OF THE LEVATOR MUSCLE

The movements of the upper lid are partly voluntary and partly involuntary. The levator muscle, which lifts the upper lid, and the orbicularis, which closes the eye, are both synchronized physiologically with the elevators and the depressors of the globe. The associated movements of the lid and the globe are of four types.

1 Up and down movements. During the waking hours the action of the levator is automatically synchronized with the continuous up and down movements of the globe, while the orbicularis assumes a passive role.

2 Winking movements. Winking is an involuntary act, executed independently of the extraocular muscles, in which the action of the levator is synchronized with that of the orbicularis, so that the former relaxes while the latter contracts and vice versa.

3 Bell's phenomenon. During sleep the upper lid moves down and the globe moves up. Here the synchronous up and down movements of the lid and globe during the wakeful hours are broken, so that now the superior rectus contracts, the levator relaxes and the orbicularis contracts to close the lids.

4 The blink reflex. This is a sudden, firm closure of the eyelids, in which the superior rectus contracts to pull the globe up, the levator relaxes and the orbicularis contracts suddenly to close the lids. It may be initiated involuntarily by objects approaching the eyes suddenly, loud

sounds or sudden flashes of light. Its physiologic basis is similar to Bell's phenomenon except that in blinking the orbicularis contracts more actively and completely.

Physiologically, Muller's muscle seems to be an auxiliary elevator of the upper lid. Anatomically, it serves as one of the attachments of the levator. Phylogenetically, it is a vestigial structure, which manifests itself functionally in man, both by overaction and by paralysis.<sup>49</sup>

### SURGICAL TREATMENT OF PTOSIS

Undoubtedly, the incidence of ptosis has remained the same throughout the ages. Yet the ancients seemed to ignore the subject entirely in their writings. According to Valude,<sup>50</sup> the only surgical procedure to survive from antiquity is the ancient Arabian operation of excising an oval piece of skin from the upper lid.

### CLASSIFICATION OF OPERATIONS FOR PTOSIS

The eighty or more surgical procedures<sup>51</sup> designed for the cure of ptosis may be divided into three groups.<sup>52</sup>

1 Suspension of the upper lid from the brow, thus utilizing the action of the frontalis muscle for lifting the lid.

2 Attachment of the upper lid to the superior rectus, thereby replacing the action of the levator by the lifting power of the superior rectus.

3 Enhancement of the normal action of the levator by advancing, tucking or resecting this muscle.

<sup>49</sup> Overaction of Muller's muscle of the upper lid occurs whenever the sympathetic nervous system is stimulated, as in fright or with hyperthyroidism or the acute phase of Horner's syndrome. This overaction is characterized by (1) a widening of the palpebral fissure, (2) apparent exophthalmos, (3) infrequent winking, (4) lid lag and (5) difficulty in everting the upper lid. After thyroidectomy in cases of hyperthyroidism, when overaction of the sympathetic nerve supply stops, the lid usually returns to its normal position, and the appearance of exophthalmos disappears. With paralysis of the cervical sympathetic fibers, Muller's muscle is relaxed, resulting in slight ptosis and apparent endophthalmos. Associated with the ptosis is narrowing of the pupil and diminution of sweating on the side of the lesion. Ptosis due to paralysis of Muller's muscle is slight and amounts to not more than 3 or 4 mm and is "cured" temporarily by the instillation of cocaine eye drops, which causes contraction of Muller's muscle by acting directly on the smooth muscle fibers themselves.

<sup>50</sup> Valude, cited by Wood.<sup>104</sup>

<sup>48</sup> Stevens, G. T. *Motor Apparatus of the Eyes*, Philadelphia, F. A. Davis Company, 1906, p. 81. Spiegel, E. A., and Sommer, I. *Neurology of the Eye, Ear, Nose and Throat*, New York, Grune & Stratton, Inc., 1944. Rea, R. L. *Neuro-Ophthalmology*, St. Louis, C. V. Mosby Company, 1938, p. 80.

*Utilization of the Frontalis Muscle*—Dransart<sup>53</sup> was the first to conceive of producing cicatricial bands between the upper lid and the frontalis muscle. He used catgut sutures beneath the skin between the upper border of the tarsus and the brow. After Dransart's publication, a number of operations with modifications, based on this principle, were described. Pagenstecher<sup>53</sup> used silk sutures instead of catgut, Gayet<sup>53</sup> used platinum wire, Mules<sup>53</sup> used gold wire, Worth<sup>53</sup> used kangaroo tendon, and Harman<sup>53</sup> used gold chain. Other modifications were made by de Wecker,<sup>53</sup> Hess,<sup>53</sup> Landolt<sup>53</sup> and others.

These operations were a step forward in the surgical treatment of ptosis but on the whole were seldom entirely successful. All depended for their success on the development of cicatricial bands between the brow and the upper lid. In the days before antisepsis, infection usually occurred along the suture tracts, which produced firm bands of scar tissue. After antisepsis became a part of every operation, infection was rare and the operation more often a failure.

Not satisfied with the suture method of suspending the upper lid to the brow, surgeons began looking about for other means of attachment. Panus,<sup>53</sup> Allport,<sup>53</sup> Grimsdale,<sup>53</sup> Tansley<sup>53</sup> and others fashioned skin flaps from the upper lid and sutured them to the brow. Angelucci<sup>53</sup> and Sourdille<sup>53</sup> sutured the levator tendon (aponeurosis) to the brow, and Calderaro<sup>53</sup> tucked the tendon to the frontalis muscle. Machek<sup>53</sup> and, later, Reese<sup>53</sup> fashioned two flaps of the orbicularis and sutured them to the frontalis. Gifford<sup>54</sup> modified the Machek procedure to include both skin and the orbicularis in the flaps. Derby,<sup>55</sup> Wright,<sup>56</sup> Lexer,<sup>57</sup> Blair,<sup>58</sup> Wei-

ner and Alvis,<sup>59</sup> Rosenberg,<sup>60</sup> Savin<sup>61</sup> and others used fascia lata. Fergus<sup>53</sup> and Roberts<sup>53</sup> used flaps of the frontalis muscle from the brow inserted into the upper lid.

The indication for the operation utilizing the frontalis muscle occurs primarily in those cases of ptosis in which shortening of the levator or suspension of the lid from the superior rectus cannot be done because of weakness of these muscles. Some authors consider the frontalis type of operation the method of choice in all cases of ptosis, while others mention it only to condemn it. The chief contraindication to its use occurs when the frontalis muscle is weak or paralyzed. Its chief advantage is that it can be used when the levator and/or the superior rectus are paralyzed. Its chief disadvantages are that the cosmetic result is not entirely satisfactory because the brow has to be elevated to raise the lid and because the pull is not in the right direction. Also, the flaps stretch, cysts form from buried skin, lagophthalmos sometimes results, and ugly puckering scars develop in the skin of the upper lid. Good results with this operation have been reported by Savin,<sup>61</sup> Blair and associates,<sup>58</sup> Poe,<sup>62</sup> Gifford,<sup>54</sup> Kiskadden,<sup>63</sup> Derby,<sup>55</sup> Rosenberg,<sup>60</sup> Magnus<sup>64</sup> and Butler<sup>65</sup>. Savin,<sup>61</sup> who performed the operation in over 50 cases, using strips of fascia lata anchored to the frontalis muscle, stated that it is the method of choice in all cases in which the levator muscle is weak and the frontalis muscle strong. Butler<sup>65</sup> reported on the results of 31 operations, using strips of fascia lata anchored to the frontalis muscle. Of these, a perfect result was obtained in 14, with normal closure and no notching of the margin of the lid, slight overcorrection resulted in 2, a puckering angulation of the upper lid was presented in 6, and slight undercorrection remained in 5.

51 De Blaskovics and Kreiker in their textbook on operations on the eye (*Eingriffe am Auge*, Stuttgart, Ferdinand Enke, 1938) list seventy-one surgical procedures for the treatment of ptosis. There are at least ten other procedures not mentioned by them.

52 An excellent classification of operations for ptosis is given by Wood.<sup>104</sup> The historical development of the surgical treatment of ptosis has been reviewed by Foster (*Am J M Sc* **118** 700-715, 1899), Beard<sup>100</sup> and others.

53 Cited by Wood.<sup>104</sup> Beard<sup>100</sup> Elschmig, A. *Ptosisoperationen*, in *Handbuch der Augenheilkunde*, Berlin, Julius Springer, 1922, vol 1. Foster, M. L. *Am J M Sc* **118** 700-715, 1899, Grimsdale, H., and Brewerton, E. *Textbook of Ophthalmic Operations*, Baltimore, William Wood & Company, 1937, pp 34-51. Spaeth.<sup>105</sup>

54 Gifford, S. R. Machek Operation, *Arch Ophth* **8** 495-502 (Oct) 1932.

55 Derby, G. S. Correction of Ptosis by Fascia Lata Hammock, *Am J Ophth* **11** 352-354 (May) 1928.

56 Wright, cited by Grimsdale, H., and Brewerton, E. *Textbook of Ophthalmic Operations*, Baltimore, William Wood & Company, 1937, pp 34-51.

57 Lexer, cited by Butler<sup>65</sup>.

58 Blair, V. P., Brown, J. B., and Hamm, W. G. Correction of Ptosis, *Arch Ophth* **7** 831-846 (Jan) 1932.

59 Weiner, M., and Alvis, B. *Surgery of the Eye*, Philadelphia, W. B. Saunders Company, pp 323-346.

60 Rosenberg, S. Fascia Lata Transplant for Ptosis, *Am J Surg* **47** 142-148 (Jan) 1940.

61 Savin, L. H. *Surgical Treatment of Ptosis*, in Ridley, F., and Sorsby, A. *Modern Trends in Ophthalmology*, London, Butterworth & Co., Ltd., 1940, pp 573-581.

62 Poe, D. L. Ophthalmoplegia Totalis, *Am J Ophth* **16** 512-516 (June) 1933.

63 Kiskadden, W. S. *Surgical Treatment*, *Am J Surg* **27** 499-501 (March) 1935.

64 Magnus, J. A. Correction of Ptosis by Two Strips of Fascia Lata, *Brit J Ophth* **20** 460-464 (Aug) 1936.

65 Butler, R. D. W. Lexer Operation, *Tr Ophth Soc U Kingdom* **59** 579-585, 1939.

Of the many different surgical techniques advocated for utilizing the lifting power of the frontalis muscle to elevate the upper lid, the use of strips of fascia lata seems to be the method of choice, all other methods having been generally discarded or being seldom used now. The chief reasons for failure of this method are slipping of the graft, infection and weakness of the frontalis muscle.

*Utilization of the Superior Rectus Muscle*—In all operations utilizing the frontalis muscle the upper lid does not move synchronously with the globe. To meet this criticism, Motaïs<sup>53</sup> devised an ingenious operation in which he fashioned a flap of muscle tissue from the middle third of the superior rectus and sutured it to the upper lid. Parinaud<sup>53</sup> and Cannas<sup>53</sup> sutured the tendon of the levator to the superior rectus. These surgeons operated entirely through the conjunctiva. Shoemaker<sup>66</sup> and Taggart<sup>67</sup> modified the Motaïs operation by making an incision in the skin as well as in the conjunctiva. Later Kirby<sup>68</sup> did the operation entirely through the skin. Because the muscle flap sometimes pulled away after operation, Morgan<sup>69</sup> and Ellett<sup>70</sup> suggested removing a piece of sclera from the globe together with the muscle flap. Instead of using the middle third of the superior rectus, Stephenson<sup>71</sup> used the outer half of the muscle and Duverger and Velter<sup>72</sup> the inner half.

The small muscle flap sometimes slipped away after operation, resulting in failure, in other cases an exaggerated Gothic-like arch was produced. To avoid this and to produce a wider and stronger adhesion, Young<sup>73</sup> sutured the upper border of the tarsus directly to the tendon of the superior rectus. Greeves<sup>74</sup> fashioned two flaps from the upper border of the tarsus and

sutured these to the medial and lateral borders of the tendon of the superior rectus. Trainor<sup>75</sup> formed a single flap from the superior border of the tarsus and, after passing it under the tendon of the superior rectus, sutured it to the upper border of the tarsus. Jameson<sup>76</sup> made a horizontal incision through the tarsus 2 to 3 mm below its upper border and pulled the tendon of the superior rectus forward through this incision, so that the superior rectus became tucked between the tarsus and the skin. Dickey<sup>77</sup> placed a piece of fascia lata under the middle third of the superior rectus, while Weiner<sup>59</sup> and Gifford<sup>78</sup> passed it under the entire tendon of the superior rectus, each suturing the two ends of the fascia lata to the anterior surface of the tarsus. Not entirely satisfied with any of the aforementioned procedures, Wheeler<sup>79</sup> and Darier<sup>80</sup> fashioned two flaps of muscle tissue from the orbicularis in front of the tarsus and sutured them to the tendon of the superior rectus.

Most writers believe that the superior rectus operation is indicated only in those cases in which the superior rectus is intact and the levator is paralyzed. According to some authors, it should be used only when bilateral ptosis exists because of the danger of producing postoperative hypotropia and diplopia. If the cornea is anesthetic this operation is hazardous, because in sleep the lower part of the cornea is nearly always exposed, thus predisposing the eye to exposure keratitis. This complication is more likely if the elevators of the globe are weak. The chief advantage of this type of operation when it is successful is that it provides for the synchronous movement of the upper lid with the globe in looking up or down. A good lid fold develops, and good elevation of the lid is secured.

The disadvantages of this operation are as follows

66 Shoemaker, W. T. Observations on Motaïs Operation for Ptosis. Report of Three Cases, *Ann Ophth* **16** 608-615, 1907.

67 Taggart, H. J. Modification of Motaïs Operation, *Tr Ophth Soc U Kingdom* **53** 417-421, 1933.

68 Kirby, D. B. Modified Motaïs Operation for Blepharoptosis, *Arch Ophth* **57** 327-331, 1928, *Blepharoptosis—The Technique of Its Surgical Correction*, *Surg, Gynec & Obst* **70** 438-449 (Feb, no 2A) 1940.

69 Morgan, O. G., cited by Greeves<sup>74</sup>.

70 Ellett, E. C., in discussion on Trainor<sup>75</sup>.

71 Stephenson, cited by Grimsdale, H., and Brewerton, E. *Textbook of Ophthalmic Operations*, Baltimore, William Wood & Company, 1937, pp 34-51.

72 Duverger, C., and Velter, E., in Bailhant, P., Coutela, C., Redslob, E., and Velter, E. *Traite d'ophtalmologie*, Paris, Masson & Cie, 1939, vol 7, p 456.

73 Young, G. An Operation for Congenital Ptosis, *Brit J Ophth* **8** 272-275 (June) 1924.

74 Greeves, R. A. Operation for Relief of Congenital Ptosis, *Proc Roy Soc Med* **26** 478-482 (Sept) 1933.

75 Trainor, M. E. Operation for Lid Ptosis, *Tr Sect Ophth, A M A*, 1935, pp 93-97.

76 Jameson, P. C. Surgical Management with Special Reference to Use of Superior Rectus Muscle, *Arch Ophth* **18** 547-557 (Oct) 1937.

77 Dickey, C. A. Superior Rectus Fascia Lata Sling in Correction, *Am J Ophth* **19** 660-664 (Aug) 1936.

78 Gifford, S. R., and Puntenny, I. Modification of Dickey Operation for Ptosis, *Arch Ophth* **28** 814-820 (Nov) 1942.

79 Wheeler, J. M. Correction of Ptosis by Attachment of Strips of Orbicularis Muscles to Superior Rectus Muscle, *Tr Sect Ophth, A M A*, 1938, pp 130-137, *Arch Ophth* **21** 1-7 (Jan) 1939.

80 Darier, cited by de Blaskovics<sup>46</sup>.

1 The upper lid cannot move independently of the globe, so that normal blinking<sup>81</sup> is interfered with

2 Lagophthalmos is present during sleep, producing keratitis in 15 per cent of the cases<sup>54</sup>

3 The operation is useful only when the superior rectus muscle is normal

4 If the tongue of muscle slips, incomplete correction or complete failure will result<sup>46</sup>

5 An exaggerated inverted V type of arching of the margin of the lid may result, especially with the classic Motais operation<sup>54</sup>

6 Entropion, with in-turning of the lashes and abrasion of the corneal epithelium, may occur<sup>50</sup>

7 Diplopia nearly always occurs during the first few weeks but usually disappears in three to four months<sup>72</sup>

8 If fixation is maintained with the ptotic eye, the hypotropia will be exaggerated by overaction of the contralateral inferior oblique muscle<sup>81</sup>

9 The Motais operation cannot be used with very young children because of the delicacy of the superior rectus<sup>82</sup>

10 The operations done through the skin are considered difficult and produce considerable reaction<sup>79</sup>

Good results with the Motais operation were reported by de Bassa,<sup>83</sup> Truc,<sup>84</sup> Lagrange<sup>85</sup> and Motais<sup>86</sup>. Since then, this type of operation has been advocated as the method of choice by Young,<sup>73</sup> Greeves,<sup>74</sup> Taggart,<sup>67</sup> Kirby,<sup>68</sup> Tramor,<sup>75</sup> Ellett,<sup>70</sup> Wheeler,<sup>79</sup> Shoemaker,<sup>66</sup> Jameson,<sup>76</sup> Dickey<sup>77</sup> and Cordes and Fritsch<sup>87</sup>. In 1928 Kirby<sup>68</sup> reported on 12 cases of operation for ptosis with his method. In 8 the operation was successful, in 2 cases the defect was undercorrected, in 1 it was overcorrected, and in 1 case the result was a failure. In 1936 Dickey<sup>77</sup> reported on 9 cases in which he had operated with his method, with failure in 1 case. In 1943 Cordes and Fritsch<sup>87</sup> reported on 21 other cases, with good results in all.

81 Dunnington, J. H. Blepharoptosis—Its Surgical Treatment, *M Rec & Ann* **35** 880-883 (June) 1941

82 Bielschowsky, A. Lectures on Motor Anomalies of the Eyes, *Arch Ophth* **13** 751-770 (May) 1935

83 de Bassa, G., in discussion on Motais<sup>86</sup>

84 Truc, P., in discussion on Motais<sup>86</sup>

85 Lagrange, P., in discussion on Motais<sup>86</sup>

86 Motais, M. Quelques documents nouveaux sur l'operation de Motais, Paris, Angers, Germain and G. Grassin, 1907

87 Cordes, F. C., and Fritsch, U. Dickey Operation for Ptosis, *Arch Ophth* **31** 461-468 (June) 1944

The chief reason for failure in all operations utilizing the superior rectus muscle is that the adhesions produced between the upper lid and the globe pull out or become stretched after operation. Of all the various methods advocated to produce this symblepharion, the use of fascia lata seems to be the most successful and the most popular at this time.

*Resection of the Levator Palpebrae Muscle*—Bowman<sup>88</sup> was perhaps the first to perform this operation. He everted the upper lid, excised the upper edge of the tarsus with about  $\frac{1}{2}$  inch (1.27 cm) of the levator tendon and sewed the conjunctiva and the levator tendon to the cut edge of the remaining tarsus. Bowman made no differentiation between Muller's muscle and the levator tendon, but in 1896 Wolff<sup>89</sup> called attention to this difference and described an operation for resection of Muller's muscle through the conjunctiva<sup>90</sup>. In 1909 de Blaskovics<sup>91</sup> first described his operation for resection of the levator muscle. His latest procedure<sup>92</sup> consists in everting the lid with a Desmarres lid hook, reflecting the conjunctiva upward, freeing the levator and its attachments (Muller's muscle and its aponeurosis) from the pretarsal tissues and excising 10 to 20 mm of the levator muscle, together with 4 to 8 mm of the upper part of the tarsus. In 1942 Agatston<sup>93</sup> modified the Blaskovics procedure slightly. For many years Wheeler<sup>94</sup> practiced, but never published, a modified Bowman resection of the levator muscle, in which a part of the tarsus and the attachments of the levator were removed through the conjunctiva. Maddox<sup>95</sup>, after reflecting the conjunctiva, cauterized Muller's muscle and the levator tendon to shorten the attachments of the levator muscle.

88 Bowman, W. Roy London Ophth Hosp Rep **1** 34, 1859

89 Wolff, H. (a) Vorlagerung des Musculus levator palpebrae superioris mit Durchtrennung, *Arch f Augenh* **33** 125, 1896, Ueber die Sehne des Musculus levator palpebrae superioris, *Ztschr f Augenh* **13** 440-457, 1905, **15** 576, 1906

90 Wolff<sup>89</sup> also described an operation for resection of the levator tendon through the skin

91 de Blaskovics, L. Die Beseitigung der Ptosis durch Verkürzung des hintern Lidsblattes und des Lidhebers, *Klin Monatsbl f Augenh* **47** 329, 1909

92 de Blaskovics, L. A New Operation for Ptosis with Shortening of the Levator and Tarsus, *Arch Ophth* **52** 563-573 (Nov) 1923, footnote 46

93 Agatston, S. S. Resection of Levator Palpebrae Muscle by Conjunctival Route Simplified Technique, *Arch Ophth* **27** 994-996 (May) 1942

94 Wheeler, J. M., cited by Meek, R. E. Applied Anatomy of the Eye Relationship to Ophthalmic Surgery, *Arch Ophth* **26** 494-513 (Sept) 1941

95 Maddox, E. E. A New Operation for Ptosis, *Brit J Ophth* **1** 358-362 (June) 1917



In 1896 Wolff<sup>99</sup> described a simple method for shortening the levator tendon through the skin, in which the levator aponeurosis was resected after being freed from the septum orbitale, anteriorly and from Muller's muscle, posteriorly. Lapersonne<sup>53</sup> combined a resection of the levator tendon with an advancement, by suturing the cut edge of the levator tendon to the tarsus 2 or 3 mm from the margin of the lid. Elsching<sup>63</sup> resected the levator tendon in almost the same way except that he placed the incision 10 mm above the convex border of the tarsus rather than 3 or 4 mm below it. Lancaster<sup>96</sup> advocated shortening the levator through a cutaneous incision, removing a piece of skin and a piece of tarsus at the same time.

In 1883 Eversbusch<sup>97</sup> described an operation for enhancing the lifting power of the levator muscle by folding the tendon on itself. An incision was made through the skin, the orbicularis muscle and the septum orbitale, halfway between the brow and the margin of the lid, thus exposing the anterior surface of the levator tendon. The tendon was then tucked on itself by means of three mattress sutures on the anterior surface of the tarsus. Snellen<sup>98</sup> suggested two operations for tucking the levator, the first resembling the Eversbusch procedure and the other without a cutaneous incision. In the latter, he passed three sutures from the surface of the skin through the entire lid just above the tarsus, thence the needles were carried up to the fornix and then downward between the skin and the levator tendon, to emerge through the skin 2 mm from the point of entrance. When the sutures were tied, the levator tendon was tucked on itself. Wilder<sup>99</sup> and Beard<sup>100</sup> have each described an operation for tucking the levator tendon and the septum orbitale by means of two sutures passed from the tarsus to the frontalis muscle, thus combining shortening of the levator with the frontalis type of operation.

**Shortening of the Lid by Excision of a Part of It.** The ancient Arabian procedure of excising a piece of skin from the upper lid was seldom successful<sup>100</sup> because the skin stretched so as to neutralize the effect of the operation. If enough

skin was removed to get a permanent widening of the palpebral fissure, lagophthalmos, corneal ulceration and sometimes loss of the eye resulted. In 1863 von Graefe<sup>101</sup> modified the ancient Arabian procedure slightly by removing an elliptic piece of orbicularis instead of skin from the upper lid. Bowman,<sup>102</sup> apparently not satisfied with his first attempt to resect the levator through the conjunctiva, attempted two years later to shorten the levator through the skin. He incised the skin, reflected it upward and downward, excised an oval piece of orbicularis, tarsus and conjunctiva and sewed the edges together. Gillet de Grandmont<sup>53</sup> accomplished the same thing by placing the cutaneous incision 2 or 3 mm above the margin of the lid instead of 8 mm above, as was done by Bowman. Nicati,<sup>53</sup> Boucheron,<sup>53</sup> Gruening,<sup>53</sup> Theobald<sup>53</sup> and Mayou<sup>53</sup> resected a piece of the tarsus. Fergus<sup>53</sup> removed skin, orbicularis and tarsus but spared the conjunctiva. Galezowski<sup>77</sup> removed skin, orbicularis, tarsus and conjunctiva. With the possible exception of the Eversbusch operation, as advocated and modified by Meller,<sup>103</sup> none of these procedures done through the skin attained wide acceptance, and today practically all have been replaced by other methods.

**Indications.** Resection of the levator is indicated in all cases of ptosis in which this muscle is active. In all cases of complete congenital ptosis the levator is practically absent surgically, but in cases of acquired ptosis this muscle is present, even though paralyzed. In some cases the muscle can be shortened to a point where its tensile strength can be counted on to support the lid mechanically. Most authors (Wheeler,<sup>79</sup> Dunnington,<sup>81</sup> Kirby,<sup>98</sup> Wood,<sup>104</sup> Spaeth,<sup>105</sup> Weiner and Alvis<sup>59</sup> and others) agree that the levator muscle must be active, else resection of the muscle will give inadequate correction. However, de Blaskovics,<sup>46</sup> Lindner,<sup>106</sup> Jaensch<sup>107</sup> and others expressed disagreement with this opinion, maintaining that the Blaskovics procedure can be used for all types and degrees of ptosis with complete

101 von Graefe, A, cited by Beard<sup>100</sup>

102 Bowman, W. Roy London Ophth Hosp Rec. 2 111, 1861

103 Meller, J. Ophthalmic Surgery, ed 3, Philadelphia, P. Blakiston's Son & Co, 1923

104 Wood, C. A. System of Ophthalmic Operations, Chicago, Cleveland Press, 1911

105 Spaeth, E. B. Principles and Practice of Ophthalmic Surgery, ed 3, Philadelphia, Lea & Febiger, 1944

106 Lindner, K. Ueber die Ptosoperation nach Blaskovics, Klin Monatsbl f Augenh 93 1-12 (July) 1934

107 Jaensch, P. A. Zur Ptosoperation, Klin. Monatsbl f Augenh 94 183-189 (Feb) 1935

96 Lancaster, W. The Operative Treatment of Ptosis, Tr Am Acad Ophth 24 235-263, 1919

97 Eversbusch, O. Zur Operation der congenitalen Blepharoptosis, Klin Monatsbl f Augenh 21 100-107, 1883

98 Snellen, H. New Method of Treating Ptosis, Tr Ophth Soc U Kingdom 10 207-210, 1890

99 Wilder, W. H. Operation for Ptosis, Tr Am Ophth Soc 8 92-102, 1897-1899

100 Beard, C. H. Ophthalmic Surgery, Philadelphia, P. Blakiston's Son & Co, 1914, pp 230-252



satisfaction, "even when the muscle is absent," because "an apparent function develops even in those cases in which this muscle is completely paralyzed or atrophic" <sup>46</sup>

**Advantages and Disadvantages** According to Malbran <sup>108</sup> and others, shortening the attachments of the levator muscle is the best procedure for the cure of ptosis and has the following advantages

- 1 Postoperative reaction is negligible
- 2 Lagophthalmos is almost absent
- 3 The lid moves with the globe normally in all directions of gaze
- 4 The margin of the lid is not deformed
- 5 A good lid fold is produced
- 6 The procedure can be used with slight or with severe ptosis
- 7 The method can be used in cases of congenital ptosis even when accompanied with epicanthus
- 8 Backward tilt of the head or elevation of the brow does not result
- 9 There is no postoperative diplopia due to weakening of the superior rectus
- 10 The method can be used in cases in which the superior rectus muscle is weak
- 11 The winking reflex is not disturbed

The disadvantages of the operation are as follows

- 1 The operation can be used successfully only when the levator muscle is active
- 2 There is a tendency to undercorrection, especially when insufficient muscle or tarsus has been removed
- 3 Lagophthalmos may result if too much tissue is removed

**Reasons for Failure** Among the reasons advanced to explain why resection of the levator fails sometimes to give adequate correction are the following possibilities

- 1 The levator may be paralyzed or too weak to support the lid. This may be true in some cases, especially when preoperative study reveals a weak levator muscle. As previously stated, however, de Blaskovics contended that the operation may be successful even though the levator is completely paralyzed

<sup>108</sup> Malbran, J. La correccion operatoria de la ptosis palpebral, *Semana med* **2** 1456-1462 (Dec 18) 1941

<sup>109</sup> Berke, R. N. Resection of the Levator Palpebrae Muscle for Ptosis *Arch Ophth* **33** 269-280 (April) 1945, *Tr Am Ophth Soc*, **42** 411-435, 1945

- 2 The sutures may pull out after operation. This is especially likely to occur when inadequate sutures are used or when severe postoperative edema develops

3 As Hildreth <sup>47f</sup> suggested, because of the failure of most authors to differentiate Muller's muscle from the levator muscle or its tendon during resection of the levator, only Muller's muscle, which is poor surgical tissue, may be resected, rather than the levator tendon, and this mistake may sometimes be the cause of inadequate correction. I <sup>109</sup> have shown by anatomic studies and operations on cadavers that it is almost impossible to resect Muller's muscle alone in any of the routine resections of the levator muscle through the conjunctiva

4 Insufficient resection of the levator or its attachments may undoubtedly be the cause of inadequate correction in some cases. In a review of fifty-seven operations for shortening the levator muscle, I showed that only 1 or 2 mm of correction as a general rule can be secured by the Bowman-Wheeler procedure. With the Blaskovics technic a larger amount of levator tissue can be removed, giving satisfactory correction in 91 per cent of the cases <sup>110</sup>. From this it was concluded that the Bowman-Wheeler operation, which is simpler to perform than the Blaskovics procedure, should be the operation of choice for slight degrees of ptosis and the Blaskovics technic for the larger amounts

#### CRITERIA FOR THE PERFECT OPERATION FOR PTOSIS

According to Savin <sup>61</sup> and others, a successful operation for ptosis should meet the following requirements

- 1 The curve of the margin of the upper lid should overlap the cornea equally on the two sides, covering the upper part of the cornea when the lids are normally open
- 2 The margin of the lid should be a smooth curve and similar in the two eyes, with no tendency to form a notch or Gothic arch or to invert the lashes when the lid is widely open
- 3 The superior palpebral crease should correspond on the two sides
- 4 The eye should be capable of being widely opened and of shutting completely, both in forceful closure and in sleep
- 5 Normal winking should be possible
- 6 The vertical distance between the eyebrow and the margin of the upper lid should normally be the same in the two eyes

<sup>110</sup> de Blaskovics, footnotes 46 and 92. Lindner <sup>106</sup> Jaensch <sup>107</sup> Malbran <sup>108</sup>

7 The upper lid of each eye should move synchronously with the globe in all directions of gaze

8 Diplopia or disturbing heterophoria should be absent

It is doubtful whether any operation for ptosis ever completely achieved all of these requirements, especially in a case of unilateral complete congenital ptosis. Certainly, the frontalis type of operation does not give this degree of perfection, because the upper lid can be raised only by raising the brow. The superior rectus operation nearly always weakens this muscle, producing hypotropia, and leaves the lower part of the cornea exposed in sleep. Adequate resection of the levator muscle in cases of complete congenital ptosis often produces lagophthalmos in downward gaze. Therefore, in any case of complete congenital ptosis the surgeon must decide which of these criteria are the most important and which should be ignored.

To obtain a perfect cosmetic appearance and a complete functional result in a case of complete congenital ptosis, in agreement with the eight criteria listed here, must be a rare attainment. One is inclined to agree with Beard<sup>100</sup> when he stated "All who have had much experience in this branch of ophthalmic surgery will agree that the results of ptosis operations, taken all in all, are far from brilliant."

### SUMMARY

Pseudoptosis should be differentiated from true ptosis. The latter may be congenital or acquired, complete or incomplete, unilateral or bilateral. Acquired ptosis is usually due to a lesion of the nervous system and has many causes. Congenital ptosis is due to a lesion of the nucleus of the third nerve or to a developmental failure of the levator muscle. This form of ptosis usually occurs as an isolated case in an otherwise normal family, but it may be familial. Associated with congenital ptosis one may find weakness of the elevators of the globe, exotropia, esotropia, Duane's retraction syndrome or complete external ophthalmoplegia. Other associated congenital anomalies are epicanthus, blepharophimosis, abnormal inner canthus, jaw-winking, amblyopia and feeble-mindedness. The preoperative study of ptosis should include measurement of the ptosis, determination of the function of the levator muscle present, effect of cocaine on the amount of ptosis present, study of the extraocular motility, measurement of the horizontal length of the palpebral fissure, notation of the position of the upper lid folds, measurement of the vertical

width of the tarsus, determination of sensibility of the cornea and tests for visual acuity, fusion, diplopia and amblyopia.

The incidence of ptosis in the general population is not known. However, about 1 per cent of all major operations on the eye are for ptosis. The surgical treatment of ptosis can be divided into three categories: (1) utilization of the frontalis muscle to lift the upper lid, (2) substitution of the lifting power of the superior rectus muscle for that of the levator muscle, (3) enhancement of the lifting power of the levator muscle by shortening it. The success of the frontalis type of operation depends on the formation of cicatricial bands between the frontalis muscle and the upper lid. To create such bands, surgeons have used surgical gut, silk, kangaroo tendon, fascia lata, gold or platinum wire or gold chain. Other material consists of skin and/or orbicularis muscle from the upper lid or of the levator tendon. Some surgeons still consider this type of operation the procedure of choice, but most operators resort to this procedure only when the superior rectus or the levator palpebrae is too weak to support the lid. Its chief disadvantage lies in the puckering which occurs in the skin of the upper lid and the fact that the pull in lifting the upper lid is in the wrong direction.

The success of the operation utilizing the superior rectus muscle depends on the formation of cicatricial bands between the superior rectus and the upper lid. These may be formed by suturing a slip of the superior rectus to the tarsus or by attaching the tarsus or the levator tendon to the superior rectus. Other material used is strips of fascia lata or orbicularis from the lid, which are sutured to the superior rectus. The chief advantage secured by this operation is the excellent synchronization of movements of the upper lid with those of the globe in looking up and down. The chief disadvantage is lagophthalmos in sleep and the formation of a notch in the upper lid.

Resection of the levator muscle is the operation of choice when this muscle is not completely paralyzed. The levator may be shortened either by resection or by tucking a part of it through the conjunctiva or through the cutaneous routes. The chief advantage of this method is that it gives a natural appearance to the upper lid, with good elevation. The chief disadvantage is that it can be used only in cases of incomplete ptosis.

Anatomically, the upper lid is made up of seven layers of tissue, namely, skin, orbicularis, septum orbitale, orbital fat, levator aponeurosis, Muller's muscle and conjunctiva. Special attention should be paid to the levator aponeurosis and

Muller's muscle, for these structures must be identified in every operation of resection of the levator muscle. The physiologic movements of the upper lid may be divided into four groups, namely, (1) movements of the lid with the globe in looking up and down, (2) winking movements to moisten the cornea, (3) Bell's phenomena and (4) the blink reflex. Besides preserving each of these functions intact, every operation for ptosis should produce a good cosmetic appearance. Too much stress should not be placed on securing a good cosmetic result at the expense of normal function of the lid, else the cornea may suffer from exposure and ulceration.

## CONCLUSION

Of the eighty odd surgical procedures advocated for the cure of ptosis, none is entirely satisfactory in all cases. As a general rule, resection of the levator palpebrae muscle is the operation of choice when this muscle is not paralyzed. Next in the order of preference is one of the operations designed to support the upper lid from the superior rectus muscle. If this muscle is weak or parietic, the frontalis type of operation may be utilized. In all operations for ptosis the functional result and the cosmetic appearance of the upper lid must be carefully considered.

430 Union Street

## News and Notes

EDITED BY DR W L BENEDICT

### GENERAL NEWS

#### AMERICAN BOARD OF OPHTHALMOLOGY

Owing to transportation difficulties, the examination originally scheduled to be held in Los Angeles, Jan 28 to 31, 1946, will be held in San Francisco, June 22 to 25, inclusive.

The following additional examinations will be held in 1946: Chicago, January 18 through 22, New York, April 10 through 13 (approximately), Chicago, October 9 through 12.

The officers for 1946 are: chairman, Edward C Ellett, M D, Memphis, Tenn; vice chairman, Georgiana D Theobald, M D, Oak Park, Ill; secretary-treasurer, S Judd Beach, M D, Portland, Maine; assistant secretary, Theodore L Terry, M D, Boston; consultant, Walter B Lancaster, M D, Boston.

**Surgery List**—A new ruling requires that previously accepted candidates mail their surgery lists to the office of the Board at least sixty days prior to their examination. All new applicants are now required to send their list with application.

**Ninth Annual W Thornwall Davis Post Graduate Course in Ocular Pathology, Orthoptics and Surgery**—The ninth annual Wm Thornwall Davis Post Graduate course in Ocular Pathology, Orthoptics and Surgery will be given at the George Washington University School of Medicine, Washington, D C, Feb 4 to 9, 1946. The course is limited to 30 registrants.

The course in pathology will be given by members of the staff of the Army Institute of Pathology: Colonel J E Ash, M C, USA, director of the Institute, Helenor Campbell Wilder, Captain Joyce Morris, M C, A U S, and Lawrence Ambrogio.

The instructors for the course in surgery will be Dr Ernest Sheppard, professor of ophthalmology, Dr Ronald A Cox, Dr Richard W Wilkinson, Dr Sterling Bockoven, Dr C R Naples, Dr M Noel Stow and Dr J Spencer Dryden.

Instructors for the course in orthoptics will be Dr Frank D Costenbader, Mary Everist Kramer, Louisa Wells, Dorothy R Bair, Alice L McPhail and Marjorie Enos.

**Bequest to College of Physicians of Philadelphia**—By the will of the late Dr Paul L Sartain, of Philadelphia, the sum of \$5,000 was bequeathed to the College of Physicians of Philadelphia, in trust for the creation of a "Library of Ophthalmological Illustrations." The trustee is to acquire by purchase or through gifts to the college, drawings and paintings delineating faithfully and accurately, as well as artistically, the ocular structures. High class reproductions of illustrations in the ophthalmologic field, as made by photographic or other methods, may be accepted, and photographs, lantern slides and films of any kind for projection on the screen may be selected. All acceptable specimens are to be properly mounted and catalogued and so arranged as to be readily consulted and used by the fellows of the College and other accredited visitors. No efforts should be spared for the careful handling and preservation of such a library.

In addition, Dr Sartain provided that "if at any time there should be a surplus of income from the fund, such surplus may be used for the preparation of illustrations of interesting cases submitted by those unable to bear the expense of their delineation, but such illustrations shall become the property of the college and be included in the Sartain library."

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

## Bacteriology and Serology

SEROLOGIC STUDIES IN ACUTE EYE DISEASES C  
C GRAY and W A MOOR, *Am J Ophth*  
28:180 (Feb) 1945

Gray and Moor give the following summary

"1 The sera of 16 eye patients were used in the manner of the Neufeld test to determine the presence of an agency that would produce a nonspecific capsular swelling of Type XXVII pneumococcus

"2 Two cases showed a positive reaction

"3 The etiology of these two cases was determined to be an organism in the gram-negative or the gram-positive groups

"4 After removal of the cause of the choroiditis, the test became negative" W S REESE

ANTERIOR MEGALOPHTHALMOS AND ARACHNODACTYLY W V STEPHENSON, *Am J Ophth* 28:315 (March) 1945

Stephenson reports a case of arachnodactyly with anterior megalophthalmos. Emphasis is given to the genetic aspects of the disease. There are many variations of anterior megalophthalmos, owing to the infinite disturbances in the genes. The term anterior dysophthalmos is suggested for the condition

W ZENTMAYER

## Congenital Anomalies

OCULAR MALDEVELOPMENT IN EXTREMELY PREMATURE INFANTS. RETROLENTAL FIBROPLASIA VI GENERAL CONSIDERATION T L TERRY, *J A M A* 128:582 (June 23) 1945

Over 10 per cent of the infants born very prematurely, with a weight of 3 pounds (1,306 Gm) or less at birth, can be expected to be blind because of retrolental fibroplasia. If this incidence continues, at least 600 cases will occur annually, thus increasing materially the number of the blind

The typical characteristics of retrolental fibroplasia are an opaque, vascularized membrane behind the lens, microphthalmos, shallow anterior chamber, fetal blue color of the iris, thin ciliary processes in front of the opaque tissue, searching nystagmus, apparent photophobia, persistent hyaloid artery, and, often, retinal detachment

The basis of the disease lies in the presence of a functioning hyaloid artery-tunica vasculosa lentis system in all infants born even three or four weeks prematurely

Of all the probable causes listed, precocious exposure to light is considered the most tenable, and preventive measures should be taken

For prevention, mydriatics and miotics should be used, but if these are considered too drastic the infants should be kept in a dark room with a red light and the eyes covered adequately during examinations and nursing care

Treatment consists in preventing the most common complications, glaucoma and posterior synechia, by use of miotics and mydriatics. Surgical therapy and irradiation have proved unsuccessful. However, a surgical attempt to establish a new vascularization of the ciliary body with the episclera is being made, with some beneficial results

W ZENTMAYER

TOTAL ALBINISM OF THE EYES. REPORT OF A CASE O CORREA NETTO, *Arq brasil de oftal* 7:13 (Feb) 1944

Netto reports the case of a man 22 years of age with total depigmentation of the eyeballs. The patient has a brother and a maternal uncle who are albinos. The rest of the family, including several brothers of the patient, are normal. The function of the retina of albinos is not involved. Dark adaptation and perception of colors are normal. Avitaminosis A and B play no role in albinism. The condition is familial, hereditary recessive and dominant and is favored by consanguinity. Marriage of albino persons should be interdicted for eugenic reasons

W ZENTMAYER

## Conjunctiva

AMYLOID DISEASE OF THE CONJUNCTIVA N B ELLES, *Am J Ophth* 28:486 (May) 1945

Elles reports a case of amyloid disease of the conjunctiva and concludes that amyloidosis may manifest itself in the conjunctiva as a primary and perhaps as a secondary, disease

The fact that in most cases reported the disease has followed or complicated trachoma need not mean that trachoma is a factor in its development, for in the majority of cases of trachoma amyloidosis does not occur. The geographic location of most cases of ocular involvement, that is, the Baltic states, Russia, Japan and China, where deficiency diseases are more prevalent would indicate that deficiency may be a factor. Biochemically, the process of amyloid deposit appears to be a disturbance in endogenous protein metabolism, in which the rate of formation of catabolic products exceeds the ability of the tissues to dispose of them. Histologically, the

evidence points to primary involvement of the phagocytic reticuloendothelial cells, whose location is exactly in the places where amyloid is constantly seen. It might be desirable to abandon the term "degeneration" and to refer to the condition as amyloid disease. W ZENTMAYER

**SELO-INFLECTED CONJUNCTIVITIS. AN ACCOUNT OF CASES PRODUCED BY THE JEQUIRITY AND CASTOR OIL SEEDS. E J SOMERSET, Brit J Ophth 29: 196 (April) 1945**

Of 31 patients seen, the condition was unilateral in 19 (right eye only in 8 and left eye only in 11) and bilateral in 12. All were Indians, none of whom had gained the rank of commissioned officers. They came from widely separated units. It was thought that in the majority of cases the condition was due to the use of the castor oil or the jequirity seed. Typically, the patient keeps the eye closed and frequently has a guilty and sulky appearance. Three main clinical types are seen: subacute, hyperacute and chronic.

The author describes a personal experiment to show that the inner seed of the castor oil plant is capable of producing conjunctivitis. The castor oil plant and the jequirity plant are described, and the clinical signs, pathologic diagnosis, differential diagnosis and treatment are discussed.

The article is illustrated. W ZENTMAYER

**Cornea and Sclera**

**RECURRENT EROSION OF THE CORNEA. P A CHANDLER, Am J Ophth 28: 355 (April) 1945**

Chandler recognizes two types of recurrent erosion of the cornea: the macroform and the microform. He suggests use of the ophthalmoscope with a +4.00 D lens to detect the lesion and believes that damaged endothelium may cause the persistent epithelial edema. He recommends the use of boric acid ointment (10 per cent) at night for the microform type and scraping the cornea and chemical cauterization of the denuded area for the macroform type.

W S REESE

**EPIDEMIC KERATO-CONJUNCTIVITIS IN THE MIDDLE EAST. CLINICAL AND EXPERIMENTAL STUDY. A FEIGENBAUM, I C MICHAELSON and W KORNBLUTH, Brit J Ophth 29: 389 (Aug) 1945**

Three hundred and eighty-one cases of keratoconjunctivitis were investigated in the Middle East, chiefly in Palestine. The majority of these cases occurred during epidemics. In the Middle East the beginning of the rainy season appears to be the period of maximum incidence of the disease. In Palestine the disease, although now

occurring inland, first manifested itself in the coastal plain. This is in accordance with observations in other parts of the globe.

In some cases trauma appeared to play a definite role in determining the onset of the condition. The involvement of lids, conjunctiva, regional glands and cornea formed a well defined clinical picture, differentiable for the most part on clinical grounds from swimming pool conjunctivitis, vernal conjunctivitis, trachoma, influenzal conjunctivitis and herpes cornea. In 60.4 per cent of cases the cornea was involved. In the cases without corneal lesions the diagnosis was made on the clinical picture, the absence of bacteria, typical smears and the occurrence during epidemics.

The mildest forms of therapy proved the best. Douchings with cool water, instillation of epinephrine hydrochloride (1:1,000) and, if necessary, use of cocaine or atropine drops were the most satisfactory remedies. Energetic treatment prolonged the course of the disease and caused gross changes in the conjunctiva. Histologic examination of the human conjunctiva showed flattening of the epithelium, pronounced capillary dilatation and edema in the subepithelial tissue, subepithelial infiltration with lymphocytes and large mononuclear cells, multiple mitoses and, in cases of the chronic type, considerable hypertrophy of the papillae.

Histologic examination of a rabbit's cornea inoculated five days previously showed the typical lesions of macular keratitis. Experiments with rabbits confirmed the specific infective nature of the causal agent. This agent was not infective for mice with different methods of inoculation.

Tissue culture and filtration experiments showed that the infective agent is a filtrable virus. Clinical immunity was apparently present in the blood of convalescent patients.

Epidemic keratoconjunctivitis is a specific disease of the conjunctiva and cornea, caused in all probability by a filter-passing virus, which can produce a similar condition in the cornea of the rabbit. The disease has its own well defined epidemiologic and clinical features. Treatment must not be energetic. Douching with cool water and instillation of epinephrine and, if necessary, cocaine and atropine drops are the most helpful remedies. W ZENTMAYER

**BILATERAL MARGINAL DYSTROPHY OF THE CORNEA. J F BALZA and F K CRAMER, Arch de oftal de Buenos Aires 19: 73 (Feb) 1944**

A case of bilateral marginal dystrophy of the cornea (keratoectasia) is described, in which spontaneous rupture of Descemet's membrane, with subsequent improvement in vision, occurred in the right eye. Prior to the accident the upper segment of the cornea was prominent and extremely opaque. After rupture of Descemet's



membrane, the cornea was flattened and became almost transparent. Visual acuity improved from 1/10 to 10/10, with a correction of —2.00 D sph —2.00 D cyl, axis 90.

The authors point out that the good results of the accidental rupture in this case suggest that a discussion of Descemet's membrane might be accomplished purposely in the treatment of this condition.

The article is illustrated, and a bibliography is furnished.

H F CARRASQUILLO

BLUE SCLEROTICS ASSOCIATED WITH BONY DEFECTS IN THE NOSE E CHAN, Chinese M J 63: 55 (Jan) 1945

A Chinese girl aged 18 years, in addition to blue sclerotics, had a cystic tumor which occupied the entire nasal fossa, apparently invading the ethmoid and sphenoid sinuses. There were pressure changes in the surrounding bony structures. The left eye was proptosed and was later enucleated. The sclera was from one-third to two-thirds the normal thickness but was of unequal tenacity. There was a slight decrease in the number, but no change in the size, of the fibers. There was thinning of the cornea.

W ZENTMAYER

SCLERAL ABSCESS F M LEE, Chinese M J 63: 60 (Jan) 1945

Lee reports 2 cases of scleral abscess. The first case was that of a boy aged 8 years. After an iridectomy the patient tore off the surgical dressings and rubbed the eye. The abscess developed one week later. In the second case, that of a young man, the abscess developed one month after an iridectomy.

W ZENTMAYER

TUBERCULOMA OF THE SCLERA K S SUN, Chinese M J 63: 67 (Jan) 1945

Tuberculoma of the sclera was noted in a young Chinese woman. The growth was excised and subjected to histologic examination. Clinical studies indicate that it was secondary to a tuberculous process in the lung. A brief review of some of the reported cases is incorporated. The mode of infection and the question of diagnosis are briefly discussed.

W ZENTMAYER

KERATOCONUS REPORT OF A CASE W S MAO, Chinese M J 63: 90 (Jan) 1945

Keratoconus was observed in the right eye of a man aged 37. Both eyes were affected with trachoma stage III. The right eye also had concomitant convergent strabismus—vision was limited to perception of light. The case is of interest because of the rarity of the keratoconus in the western and northern part of China.

W ZENTMAYER

## General

A DISCUSSION OF OCULAR MALINGERING IN THE ARMED SERVICES A C UNSWORTH, Am J Ophth 28: 148 (Feb) 1945

Unsworth discusses malingering in the armed services, its types and the various tests for its detection. He recognizes several forms of malingering, which may be classified as positive, in which the man attempts to prove his falsification, and negative, in which he falsely denies the existence of a history or physical signs of existent disease or injury.

There is a significant relationship of malingering, war neurosis and morale among the troops. High morale depends on several local factors in the soldier's environment: healthy training conditions, food of adequate amount and good quality, sufficient exercise, supervised sports and other diversions, medical care that inspires confidence, good relationship between the men and their officers, rigid discipline and drilling, which inspires a sense of group security, talks to groups of soldiers on the psychological aspect of fear and its understanding, and, most important, a clear perspective and appreciation of the ideology for which the war is being fought and the value to the individual, his family, the nation and the world of maintaining this ideology.

W ZENTMAYER

OPHTHALMOLOGY IN PARIS DURING THE WAR P PRELAT, Am J Ophth 28: 1073, (Oct) 1945

Prelat gives an interesting account of ophthalmologic work in Paris during World War II. He presents numerous brief reports of cases and of theses submitted to the Ophthalmological Society of Paris, the last bulletin of which carried reports from October to December 1939.

W S REESE

THE EYE OF THE WEST AFRICAN NEGRO J. G. SCOTT, Brit J Ophth 29: 12 (Jan) 1945

A study of the eyes of 1,000 Gambian school children and 1,100 Gambian, 300 Gold Coast, 300 Nigerian and 300 Cameroon soldiers, in addition to hospital patients and outpatients seen at a West African military hospital over a period of eighteen months, was made. Noteworthy differences were found between the eyes of Africans and those of Europeans.

A summary follows.

Pigment of the interpalpebral conjunctiva and a ring of pigment around the limbus are normal.

Vascularity of the cornea beyond the ring of pigment is pathologic and is most frequently caused by trachoma. This condition should be excluded before pannus is attributed to tropical disease.



The Negro fundus is red, not chocolate or slate gray, in appearance

A 2 per cent solution of homatropine hydrobromide and/or cocaine hydrochloride is not an efficient mydriatic

Nebulas in the substantia propria are common and are most frequently caused by onchocerciasis and trachoma

Iritis is caused by onchocerciasis and by trypanosomiasis, as well as by more usual diseases

Microfilarias are not uncommon in the aqueous, where they are well tolerated. The most common, if not the only one, is *Onchocerca volvulus*

The value of removal or destruction of nodules containing the adult *Onchocerca volvulus* is doubted, as the nonencapsulated worm plays an important part in infection and in producing ocular complications

W ZENTMAYER

EYE DISEASES IN THE EAST J MINTON, Brit J Ophth 29 19 (Jan) 1945

Minton gives a brief account of the ophthalmic diseases of the natives of Iraq. Epidemics of infective ophthalmias occur regularly every year. They begin in May and last until December. About 60 per cent of the population is thought to be infected with trachoma. The British troops showed a very low incidence of infective conditions of the eye. There was no epidemic of conjunctivitis. The Indian troops had a much higher incidence of conjunctivitis than the British. Mucopurulent conjunctivitis of a severe type associated with corneal ulceration was of frequent occurrence. The Indian and Ceylonese troops and the natives suffered from epidemic punctate keratitis, but no cases were seen among the British troops. There were no cases of gonococcal conjunctivitis among the British or the Indian troops

W ZENTMAYER

### General Diseases

ARIBOFLAVINOSIS I MANN, Am J Ophth 28 243 (March) 1945

Mann reports a case of ariboflavinosis in a man aged 29 years. The right eye showed severe conjunctival injection, the main vessels being intensely engorged. The limbal plexus was full. There were no new conjunctival vessels. The cornea showed marginal vascularization and opacities in the substantia propria. The vascularization was distinctive. It was in the form of parallel, radially arranged loops springing from the apexes of the loops of the limbal plexus and extending in three arcades beyond this slightly more than halfway to the margin of the pupil. The vessels were so engorged with blood that they appeared to stand out from the surface. They were mostly subepithelial, but in the region

of the opacities in the cornea they had penetrated the substantia propria to about one-half its thickness. They extended all around the circumference of the cornea. The opacities were coarse, whitish patches, located in the subepithelium. Both eyes were affected, but to a different degree.

The patient had been on a diet which contained no fruit and supplied green vegetables once a week.

With a proper diet and the administration of multivitamins, the cure was dramatic.

W ZENTMAYER

HERPETIC DISEASES OF THE EYE IN THE LIGHT OF MODERN VIRUS INVESTIGATIONS M GRUTTER, Arch Soc de oftal hispano-am 3. 494 (Nov-Dec) 1943

The herpes virus may be the causal agent in the following processes: herpes of the palpebral margin, vesicular keratitis in its varied forms, dendritic keratitis in its variations, geographic keratitis, stellate keratitis, filamentous keratitis, recurrent corneal erosions, striate keratitis, circumscribed parenchymatous keratitis, diffuse parenchymatous keratitis, herpetic endothelial keratitis and herpes of the irises. Epidemic keratitis and nummular keratitis may have some connection with the virus. An explanation of how these conditions are brought about by the action of the virus toxin is given.

H F CARRASQUILLO

### Hygiene, Sociology, Education and History

PATRON SAINTS OF THE EYES AN OUTLINE F L P KOCH, Am J Ophth 28. 161 (Feb) 1945

Koch recounts the histories of the various saints and the ocular conditions which they were thought to influence. He stresses the importance of sympathetic understanding of faith in such beliefs.

W S REESE

A CENTRAL OPHTHALMOLOGICAL INSTITUTE FOR THE UNITED NATIONS A LOEWENSTEIN, Brit J Ophth 29 6 (Jan) 1945

Loewenstein suggests a common central institute of ophthalmology for the United Nations. Similar institutes for other specialties might follow. They may be distributed over the large towns of the Nations according to the need and the availability of suitable teachers. In the near future the common budget of the Allied Nations will be considerable. The idea of a common education must not be forgotten. Central medical institutes are a part of it, and all nations will enjoy the fruits of their work. A blueprint of such an institution is offered, and the details of equipment are given.

W ZENTMAYER

WORD BLINDNESS, ITS CAUSE AND CURE  
R HALL, Brit J Ophth 29:467 (Sept)  
1945

The author suffered from word blindness, being unable to read up to the age of 15, i.e., prior to puberty (Did altered thyroid function have something to do with this change?) The theory has been advanced by Stout that the chief instrument used by the blind in perceiving the shape and size of objects is the hand, or, rather, the two hands. This is accomplished by what may be called synthetic touch, because it yields a total simultaneous impression of all, or many, parts of the object. Second, the finger tips may explore the parts and contours of the object by gradually moving over them. This may be called the active touch, or the analytic touch, because it analyzes or breaks up into a series of successive impressions what synthetic touch presents as a simultaneous whole. This concept naturally leads to the question whether development in definiteness of the perception of letter order, or words, may not be essentially due to the intimate union and cooperation of synthetic and analytic vision. All words must be analyzed or broken down into their smaller parts and then synthesized again by association. When the letters are thoroughly known, two letter words should be learned. These should be learned first of all by analytic vision, that is, by splitting them up into, or regarding them as, two separate letters, until sufficient synthetic vision is acquired to fuse them by association or to see them as a single unit. Passages in books should then be used, the patient picking out all known two letter groups, such as those underlined in "*Now this is the best method*". This is a form of analytic vision which, by breaking down words, will gradually extend synthetic vision so that it will gradually absorb even the longer words thus broken down. For "now" is no longer a meaningless collection of letters—it is the word "no" with a letter after it—that is, in its written form it has acquired a definite personality which differentiates it from other words, and all thought has to move by way of differentiation.

When all two letter words have been thoroughly mastered in this way, the same procedure should be followed with three letter words, and then with four letter words, in order gradually to extend synthetic vision. W ZENTMAYER

THE ONE-EYED WORKER J MINTON, Brit J Ophth 29:472 (Sept) 1945

Minton divides one-eyed people into two groups: those who have been without an eye since childhood and those who have lost the vision of an eye in adult life as the result of disease or injury. Persons of the first group are in no way handicapped and have full confidence in

the carrying out of their work. A person of the second group takes a little time to adjust himself to the new visual condition. This adjustment requires from a few weeks to several months. The degree of depth perception acquired depends on several factors: intelligence and previous experience in judging distance, age, sex and whether the eye lost was the dominant eye. The time required for the regaining of confidence to return to work should rarely exceed two to three months, but the greater number of men stay away from work for periods varying from six to nine, or even ten months. The reasons for this are fear and lack of confidence, compensation and litigation difficulties and the unwillingness of firms to employ one-eyed workers. The occupation suitable for a one-eyed person depends on the vision of the good eye. With vision of 6/6 or 6/9, all occupations involving close work can be performed with comfort. If visual acuity is 6/12, occupations requiring constant close work are inadvisable. If vision is less than 6/12, such work as gardening, farming or domestic service is suitable.

W ZENTMAYER

### Injuries

REPORT OF AN EYE INJURED BY LIGHTNING.  
L B SHEPPARD, Am J Ophth 28:195  
(Feb) 1945

A youth aged 18 years was struck by lightning and remained unconscious over four hours. On the right side there were marked edema of the lids, moderate chemosis of the conjunctiva and complete external ophthalmoplegia. The cornea showed a whitish gray opacity, with cloudiness in the posterior half of the cornea. Vision was limited to light perception, and tension was normal. There was retinal edema about the optic papilla. On the twenty-ninth day there were localized detachment of the retina, two small areas of choroiditis in an area of retinal edema and a fibrous band in the posterior part of the vitreous. On the forty-fifth day a second area of detachment of the retina was noted. About one week after the accident an acute attack of iridocyclitis developed. Two months later there were opacities in the posterior cortex and the vitreous and complete detachment of the inferior portion of the retina.

W ZENTMAYER

INTRAOCULAR FOREIGN BODY OF INFREQUENT LOCALIZATION AND PROLONGED TOLERANCE  
J M VILA ORTIZ, Arch de oftal de Buenos Aires 19:91 (Feb) 1944

Vila Ortiz describes a case in which a foreign body was lodged in the papilla. According to him, this is the third case of the kind reported in the literature. A man 36 years of age fell

and received an injury to the left eye. The eye showed hyphemia and turbidity of the media, but no portal of entry of any foreign body was found. The roentgenographic examination also failed to show its presence. The giant magnet was also used for diagnosis, with negative results. After the media cleared, a grayish mass 2 by 2.5 mm, taken to be a foreign body, was observed in the papilla. The eye was blind. A second roentgenogram, taken with the Sweet method, corroborated the diagnosis. The only sign of intolerance was optic neuritis. No endeavor was made to remove the foreign body. Four years later the eye was quiet. Foreign bodies in this location are well tolerated and do not require extraction, nor is enucleation indicated if the foreign body is chemically inert and nonmagnetic. The article is illustrated.

H F CARRASQUILLO

### Instruments

AN OPHTHALMIC SLIDE RULE TIENYUNG MIAO, Chinese M J 63:80 (Jan) 1945

On each side of the rule there are several graduations from which may be determined the interpupillary distance, the near point of convergence, the binocular parallactic angle, the angle of convergence, the accommodative power, the tangent rule, the meter angles, etc.

The article is illustrated. W ZENTMAYER

### Lacrimal Apparatus

DACRYORHINOSTOMY N BELMONTE GONZALES, Arch Soc oftal hispano-am 4:33 (Jan-Feb) 1944

When the lacrimal sac has been removed and the canaliculi are intact, the operation of Arruga, canaliculorhinostomy, is indicated.

When there is absence of the lacrimal sac and the canaliculi, the operation of dacryorhinostomy is indicated. This procedure is also used when the obstruction is in the canaliculi before they empty into the sac.

The operation which the author terms dacryorhinostomy, and which consists in opening a fistulous passage between the lacus lacrimalis and the nasal cavity, is described in detail, and the procedure is illustrated with colored plates.

H F CARRASQUILLO

### Lens

TRANSPARENCY OF THE LENS FOLLOWING TRAUMATIC CATARACT H J STERN, Brit J Ophth 29:48 (Jan) 1945

The left eye of a Negro aged 25 had been injured by a flying particle of stone. Several hours after the injury an anterior capsule cataract was

present. Exactly the same abnormality was seen in the other eye. Three days later a brilliantly white, mushroom-shaped mass was protruding from the lens into the anterior chamber of the left eye. The roentgenogram was noncontributory. Thirteen days after the injury, only a few gray capsular opacities were left, and a feathery posterior cortical cataract was seen. On the twenty-third day the eye was again white and perfectly normal except for the unchanged anterior capsular cataract and a fine opacity near the center of the cornea. Vision was 6/6. The eye was emmetropic. The author analyzes the various possibilities in explanation of the case.

W ZENTMAYER

### Lids

THE ORIGIN AND PURPOSE OF BLINKING A HALL, Brit J Ophth 29:445 (Sept) 1945

This inquiry was begun some years ago in order to find out to what extent the rate of blinking is reduced in chronic encephalitis. In the course of preliminary tests on normal persons certain unexpected points were noted. All persons tested were unaware that their blinking was being watched, in each test the surroundings and the procedure were the same for all subjects, all stimuli capable of causing local reflex blinking were excluded.

Apart from the reflex blinking seen in animals and man, which is solely for the local protection and efficient action of the eyes themselves, all blinking in man is the muscular act by which the controlling nervous center automatically shuts off the act of fixation in order to put the extramuscular reflex into full action.

Reasons for blinking may be as follows:

For self preservation, either from a threat of real danger to life coming from without through any of the sense organs or from undefined fears aroused by the surrounding conditions at the time. The former is the primitive unconditioned reflex seen throughout the animal kingdom, the latter is probably of the same origin but is conditioned in the primates by the increased security of arboreal life and in man still more, by the requirements of civilization. This type forms a large proportion of the blinking in everyday life.

For change in the direction of fixation. While some blinking is but a part of the orientation of the head and eyes in the self preservation reflex, it far more often, especially in the primates, serves either for the purpose of "looking about" or as an aid to the various purposes for which fixation is used independently.

For pauses in the act of reading aloud. These are conditioned reflexes acquired by training.

W ZENTMAYER

## Neurology

HEAD INJURIES FROM THE OPHTHALMOLOGIST'S VIEWPOINT A D ECKER and E W ANTHONY, Brit J Ophth 29:43 (Jan) 1945

The article discusses some of the newer concepts concerned with head injuries which may be of interest to the consulting ophthalmologist.

Concerning the late results of blunt head injuries, the vast majority of both civilian and military personnel return to their full duties in a matter of weeks, with proper management. The patient must be approached in an attitude of calm reassurance.

The fixed dilated pupil is an infallible sign of increased intracranial pressure. It is usually due to a laterally placed intracranial lesion on the same side, which is most often in the temporal, but may be in the frontal or the parietal lobe. The occurrence of bilateral fixed dilated pupils soon after a head injury indicates a bad but not hopeless prognosis. If the condition is associated with neurogenic hyperthermia, rapid pulse, quickly rising rectal temperature, cold skin and decerebrate rigidity, there is damage to the midbrain.

The Argyll Robertson pupil may result from a head injury. The lesion in cases in which this sign is present may be either in the central nervous system itself or in the peripheral efferent pathway to the pupil. In a study of lesions of the temporal lobe, one can use routine clinical, roentgenologic and electroencephalographic methods, as well as observation of the visual fields, speech and caloric nystagmus.

When recovery from a muscular palsy occurs within a matter of days, the nerve has been injured in a process akin to concussion, whereas if months are required, the axons presumably have been torn and have regenerated in an intact nerve sheath. If no recovery occurs, one can assume severance of the nerve, severe damage to its blood supply or such firm scarring that regeneration is prevented. Changes in the visual fields are discussed. The presence of normal visual fields does not exclude the possibility of a slowly progressive subdural hematoma overlying the optic radiations.

It has been shown that electroencephalograms, when used as an index of active cerebral abnormality after head injury, will help to estimate the extent of the cerebral damage.

W ZENTMAYER

## Ocular Muscles

ORTHOPTIC FICTIONS AND MISCONCEPTIONS L WELLS, Am J Ophth 28:890 (Aug) 1945

Wells discusses various misconceptions and differences of opinion relating to orthoptics. One

misconception is that vision in an eye with amblyopia ex anopsia cannot be improved after the sixth year of life. Such a conception is an admission that occlusion has been incomplete and of too short duration. Another fiction in orthoptics is that "alternating squints cannot be made to fuse." It is a misconception to assume that anomalous correspondence cannot exist in a patient who has visual acuity of 20/15 in each eye.

W ZENTMAYER

SOME OBSERVATIONS ON A TENDENCY TO NEAR-POINT ESOPHORIA AND POSSIBLE CONTRIBUTORY FACTORS D D STENHOUSE STEWART, Brit J Ophth 29:37 (Jan) 1945

A short period of exacting close work in special conditions of binocular dissociation is shown to cause a change of a temporary nature in ocular muscle balance at the near point (33 cm) as assessed by normal routine methods.

It is implied that muscle balance at the near point cannot accurately be stated without reference to the manner of use of the eyes preceding the assessment.

If it can be assumed that man is deficient in natural power of voluntary divergence to counteract accommodative esophoria, it follows that in the "resting" state "near point" exophoria of some degree accompanied with adequate reserve power of voluntary convergence is desirable for the comfortable performance of sustained close work.

It is further suggested that in some cases temporary disturbance of this balance and of comfortable near point effort can arise from emotional states, especially if aroused by close work and related to anxiety about its successful performance.

W ZENTMAYER

OPERATION FOR CORRECTION OF PARALYTIC EXTERNAL (LATERAL) RECTUS PALSY J P SPENCER WALKER, Brit J Ophth 29:477 (Sept) 1945

Walker reports 2 cases of paralyzes of the external rectus muscle in which a slight modification of Lancaster's operation was used. In the first case, that of a child 4 years of age, the history suggested birth injury to the right eye. The eye was amblyopic. On the twenty-fifth day after the operation the eye could be abducted fully. In the second case, that of a child 6 years of age, the left external rectus muscle had been palsied since birth. There was some postural torticollis. Immediately after operation there was an overcorrection, at the end of two weeks the power of adduction was returning and the torticollis was greatly improved. The modification of the Lancaster operation consisted in the recession of the internal rectus muscle.

W. ZENTMAYER

STRABISMUS BARBOSA DA LUZ, Rev brasil de oftal 2 31 (March) 1944

Barbosa da Luz discusses the respective indications for orthoptic and surgical therapy of strabismus. He discusses the value of determination of visual acuity, angles of deviation during ocular movements, type of strabismus, sensory condition of the retina, presence and quality of binocular vision and Worth's test of four points for the selection of either type of therapy. The author concludes that operation followed by orthoptic training is the proper therapy for strabismus. Surgical therapy alone is indicated only for patients who ask only for cosmetic correction of strabismus. W ZENTMAYER

### Operations

A MODIFICATION AND EXTENSION OF THE McREYNOLDS OPERATION FOR PTERYGIUM L STATZ, Brit J Ophth 29 193 (April) 1945

The first step of the operation is the same as that in the McReynolds method. The new direction of the displaced pterygium is such that there is no overlapping of the conjunctiva along the upper portion of the limbus. The redundant edge of the conjunctiva, between the incision and the tied silk stitch, is incised and a flap is formed, this flap is turned upward and stitched to cover the raw area of sclera and to lie along the limbus without encroaching on the cornea. A stitch from the adjacent conjunctiva biting firmly into the flap serves to obliterate a small uncovered area. The accompanying sketches show the steps of the operation. W ZENTMAYER

### Orbit, Eyeball and Accessory Sinuses

BULGING OF EYELIDS WITH EXOPHTHALMOS F F RUNDLE and C W WILSON, Clin Sc 5 31 (Aug 7) 1944

In this paper, Rundle and Wilson direct attention to the fatty swelling of the lids occurring with exophthalmos in cases of diffuse toxic goiter, giving particular attention to the clinical characteristics and the mechanism. Such swelling is not confined to patients with toxic diffuse goiter but is found with a variety of conditions characterized by overfilling of the orbit and exophthalmos. It is, in fact, simply a protrusion of the normal lid and is not due to edema of the palpebral tissues, as is generally stated. Variations in protrusion or recession accurately reflect changes in the degree of orbital filling. In wasting of the orbital tissues the eye is sunken. The lids are receded. Bulging of the lids due to prolapsing fat has a well defined clinical appearance. In the upper lid this is most evident with the eye closed, in the lower lid, with the eye open. After discussing prolapsing orbital

fat as the cause of bulging of the lids, the authors show how it is differentiated from edema of the eyelids. Further, they demonstrate the correlation between protrusion of the lid and proptosis and then discuss the mechanics of exophthalmos and protrusion of the lid. Disparity between the bulk of the contents and the capacity of the orbit may arise from a variety of clinical conditions, but some expression, such as orbital overfilling, overcrowding or disproportion, is necessary to describe their common pathologic basis. In its strict sense, exophthalmos is only one of the consequent signs. Protrusion of the lid is another. It remains for clinical investigation to determine others and so to decide which of the manifold ocular signs described in cases of toxic diffuse goiter are explicable on this simple basis. Unfortunately, "exophthalmos" is often used in an omnibus sense to describe all such cognate signs. The authors conclude that variations in the plane of the eyelids, whether they are sunken, normal or bulging, reflect corresponding variations in the degree of orbital filling, as do correlated changes in the position of the eye. The clinical characteristics of sunken and bulging lids are well defined, these, together with the exophthalmometric reading, make possible the detection of departures from the average degree of orbital filling.

J A M A (W ZENTMAYER)

UNILATERAL HYPOTONY DURING ANAESTHESIA INA BRITTAIN and G J C BRITTAIN, Brit M J 1 442 (March 31) 1945

At the Derbyshire Royal Infirmary unilateral hypotony was observed after anesthesia in 13 of a series of 300 cases. The cause was pressure exerted by the rim of a badly adjusted face mask. According to the authors, pentothal sodium is known to cause bilateral reduction in tension and tends to exaggerate the effects produced by pressure. The possibility of the occurrence of acute glaucoma in the affected eye should be borne in mind, as the lowered intraocular tension is followed by a rise above the normal, which may last for some hours. ARNOLD KNAPP

### Physiology

DYNAMIC FACTORS IN THE FORMATION AND REABSORPTION OF AQUEOUS HUMOUR J S FRIEDENWALD, Brit J Ophth 28 503 (Oct) 1944

During the last decade the problem of the aqueous has been attacked by three groups of workers, using three different techniques. Duke-Elder and his co-workers have studied the composition of the aqueous, have found the fluid to be hypertonic in electrolytes and have consequently concluded that secretory forces enter into its formation. Kinsey, Grant and Cogan



have studied the rate at which dissolved substances are exchanged between blood and aqueous, have found that this rate is greater for electrolytes than for nonelectrolytes (excluding water) and have concluded that electrolytes are secreted into the intraocular cavity, whereas diffusion and osmosis suffice to account for the rates of exchange of nonelectrolytes provided reasonable assumptions are made regarding the mechanism of outflow. Friedenwald and his co-workers have studied the mechanism of secretion in the ciliary body and have been able to formulate with some precision how the metabolic energies of this tissue are utilized for the work of secretion.

The present paper represents an effort to bring together these three independent lines of investigation. It is shown that the secretory mechanism as it is at present understood through the work of Friedenwald and his co-workers would account for the formation of an aqueous hypertonic in electrolytes, as has been found by Duke-Elder and his co-workers, and would likewise account for the higher rate of transport of electrolytes than of nonelectrolytes from blood to aqueous, as has been found by Kinsey and his colleagues. The position of the three groups of workers may be summarized as follows. Duke-Elder has concluded that the aqueous is a secretion. Kinsey agrees and specifies that it is the electrolytes in particular that are secreted. Friedenwald agrees and specifies that of the electrolytes it is primarily the cations that are secreted. W ZENTMAYER

### Retina and Optic Nerve

COMPLETE CONGENITAL PIGMENTATION OF THE OPTIC DISC W MOEHLE, *Am J Ophth* 28: 377 (April) 1945

Moehle briefly reviews the literature and reports the case of a 65 year old man with chronic glaucoma, whose right optic disk was entirely covered with brownish black pigment.

W S REESE .

SHEATHING OF THE RETINAL VEINS IN MULTIPLE SCLEROSIS C W RUCKER, J A M A 127: 970 (April 14) 1945

In a series of 50 cases of sheathing of the retinal veins, multiple sclerosis was present in 31, it was suspected in 11 cases, and there was no evidence of the disease in 8 cases. Thickening of the vascular walls at a distance from the disk is almost always indicative of disease. Venous sheathing that occurs without any other visible disease in the retina seems to have special significance. The fundal picture bears resemblance to a feature observed by a number of pathologists in sections of the central nervous system of patients who have died of multiple sclerosis, namely, an

accumulation of cells around venules. Rucker concludes that sheathing of some retinal veins is occasionally encountered on ophthalmoscopic examination of otherwise normal fundi. It is usually indicative of disease of the central nervous system, most often multiple sclerosis. The article is illustrated.

W ZENTMAYER

STARGARDT'S DISEASE. REPORT OF THREE CASES E SALGADO BENAVIDES, *Arch Soc oftal hispano-am* 4: 185 (March-April) 1944

After observing 3 patients with heredomacular degeneration, the author comes to the following conclusions. 1 Stargardt's disease is to be considered a retinal degeneration, beginning at the macula, familial in nature and of unknown cause. 2 Its characteristic progressive course is divided into three stages. In the first stage subjective manifestations appear in relation to retinal lesions. At this time the lesions are visible only on careful observation. The second stage coincides with well defined retinal lesions limited to the macular area. The third stage is characterized by pigmented and degenerated foci in extensive areas of the retina. 3 The disease seems to have a selective tendency to involvement of the retinal cones. 4 The process does not produce total blindness.

H F CARRASQUILLO

ETIOPATHOGENESIS OF "ESSENTIAL" ARTERIAL HYPERTENSION. PRESENT CONCEPTION OF PROBLEM A VILELA, *Rev brasil de oftal.* 2: 181 (June) 1944

According to Vilela, the main pathogenic factor in essential arterial hypertension is worry, emotion and subconscious conflicts. Heredity and the presence of renal and endocrine disorders are associated factors. The stage of the disease and the prognosis for the patient's life are determined by the progressive changes in the fundus of the eye as evaluated by Wagener, who places the patient according to the changes in the fundus in one of four groups.

In patients of the first and second groups the disease is in its early stages and consequently is benign. It is in the progressive, intermediate, stage in patients of the third group and is malignant in patients of the fourth group, with a prognosis of one or two years of life in 95 per cent of the cases.

W ZENTMAYER

### Trachoma

TRACHOMA VIRUS AND THE MORPHOLOGY OF INCLUSION BODIES A LOEWENSTEIN, *Am J Ophth* 28: 282 (March) 1945

Loewenstein summarizes his observations on advanced trachoma. The follicles consisted of lymphocytes, plasma cells, fibroblasts and macrophages (cystophages, Marchand). The macro-



phages contained no granules, suggesting inclusion bodies. The caps reported by Cuenod in the cells of the follicles were not found in any of the 23 cases of advanced trachoma which formed the basis of this histologic investigation. The appearance of the inclusion bodies differed in scrapings and in section. In the scrapings they showed considerable polymorphism, and individual elementary and initial bodies might be found alone in the cells. In sections encapsulated inclusion bodies with many Giemsa staining elements were found in the superficial epithelial layers. In the middle layers they were fewer, and they were absent in the deeper layers. In the subepithelial tissues, reticulum cells of fibroblast character were filled with blue and purple granules. Granules were free in the tissues—some single, others in colonies. The tarsus was found to be full of reticulum cells of fibroblast character, similar to those in the subepithelial tissues.

W ZENTMAYER

THE ETIOLOGY OF TRACHOMA. A CRITICAL REVIEW OF PRESENT KNOWLEDGE. J O W BLAND, Brit J Ophth 29. 407 (Aug) 1945

The available evidence shows that trachoma is an infectious disease, caused by a noncultivable, filtrable agent identical with the elementary and initial bodies found in the Prowazek-Halberstaedter inclusions and having a close relation to the viruses of inclusion blennorrhoea, lymphogranuloma venereum and psittacosis. There is no evidence that this agent possesses an arthropod host or that the louse is a vector of the disease, though the agent may survive for some days in the body of the louse. In what group of organisms this agent, with the other three to which it is related, is to be placed becomes largely a matter of personal choice. All four agents resemble the rickettsias in a number of points. They differ from the majority of rickettsias in not possessing an arthropod host. The four agents differ from the typical large virus in possessing initial bodies which stain blue with the Giemsa method and in showing greater pleomorphism, in forming inclusions with a basophilic matrix and in staining with Castaneda's stain. They differ from the typical rickettsias in the lack of an arthropod host, in not showing bacillary and thread forms and in forming inclusions with a matrix. The author considers that they stand in an intermediary position between the rickettsias and the large viruses and may possibly form a biologic link between them. He prefers to group them with the viruses but to give them a distinctive position as the "basophilic viruses" on account of the blue staining of their initial bodies and of the matrix of their inclusions, a reaction which distinguishes them from the larger typical viruses, which do not possess blue initial bodies and whose inclusions are acidophilic.

A bibliography is given. W ZENTMAYER

QUININE BISULFATE IN LOCAL THERAPY OF TRACHOMA. O APRIGLIANO, Arq brasil de oftal 7. 45 (April) 1944

Aprigliano observed the results of three types of therapy in three groups, of 60, 30 and 30 patients (children and adults), with trachoma. The therapy for patients in the first and second groups consisted in the expression of the conjunctival granulations with a swab soaked in a 7.5 per cent solution of quinine bisulfate and massage for two minutes, followed by the local application of a second and a third swab soaked in the same solution. The caruncle was massaged separately. A 1 per cent solution of tetracaine hydrochloride was used for conjunctival anesthesia. Local quinine bisulfate therapy was employed every other day for two weeks and twice a week thereafter until a cure was effected. An ointment which contained 6 per cent quinine bisulfate was applied locally on the days in which the local therapy was not applied. In the second group, only sulfanilamide by mouth, in proper doses, was administered. The patients in the third group had the usual therapy for trachoma which is given in dispensaries, namely, digital expression of the granulations and conjunctival massages with solutions of acid mercuric nitrate and of copper sulfate. The results of quinine therapy were the same for patients who had sulfanilamide as for those who did not. The duration of local therapy with quinine bisulfate, whether used alone or in association with sulfanilamide, was greatly shortened as compared with that for patients who had treatment with acid mercuric nitrate and copper sulfate. Quinine bisulfate, locally applied to eyes with trachoma, exerts a prompt favorable effect on the corneal lesion, the pannus and the keratic ulcers. The treatment is well tolerated. It is advisable to give short courses of quinine bisulfate at long intervals after cure, in order to prevent recurrences.

W ZENTMAYER

A STATISTICAL STUDY OF TRACHOMA AMONG IN-PATIENTS. HSIU-HSIANG CHI, Chinese. M J 63:73 (Jan) 1945

Of 2,903 patients admitted to the department of ophthalmology of the Chengtu Eye, Ear, Nose and Throat Hospital from January 1940 to December 1943, 1,305 (44.9 per cent) had a condition diagnosed as trachoma. The sex ratio was 54.6 per cent females to 45.4 per cent male. The age of 65.1 per cent of the patients ranged from 16 to 40 years. More than half the patients were affected during the most useful part of their lives. Housewives had the highest incidence, followed by students, merchants and farmers. Nearly all affected persons showed sequelae or complications, 31.9 per cent were "blind" on admission, while 22.8 per cent were so classified on discharge. In 80 per cent the cause of blindness was a lesion of the cornea due directly or indi-

rectly to trachoma. In order to reduce blindness in China, it is essential therefore to control the spread of trachoma.

Chan, in the same issue of this journal, compares the statistics for 1938 and 1939 with those presented by Chi for 1940-1943.

W ZENTMAYER

### Tumors

RECURRENT JUVENILE PAPILLOMA OF THE CONJUNCTIVA J D WALKER, *Am J Ophth* 28:751 (July) 1945

Walker reports a case of papilloma of the conjunctiva which recurred repeatedly, eleven operations being performed during five years of observation and treatment. From the literature it is evident that a papilloma may not be an innocent growth, as a number of cases are reported which show that it is capable of malignant degeneration. The tumor is best removed surgically. If roentgen radiation or radium is used, every precaution should be used to protect the lens.

W ZENTMAYER

THE MANAGEMENT OF EPIBULBAR MALIGNANCY WILFRED E FRY, *Pennsylvania M J* 48:694 (April) 1945

Fry divides epibulbar tumors into the benign, the potentially malignant and the malignant. The benign tumors are the granulomas, epithelial plaques, papillomas, lipomas, hemangiomas, lymphangiomas and dermoids, the potentially malignant tumors are the nevi and malignant papillomas and the malignant tumors are the sarcomas, the epitheliomas and precancerous melanosis.

Two cases are reported, showing, respectively, (1) that sarcoma of the limbus may remain localized at the limbus for a number of years without extensive involvement of the cornea, without intraocular extension and without distant metastasis and (2) that epithelioma of the limbus may extend into the cornea at an early stage.

W ZENTMAYER

### Vision

VISUAL SYMPTOMS CAUSED BY DIGITALIS F D CARROLL, *Am J Ophth* 28:373 (April) 1945

This is a report on 6 patients who had visual symptoms due to digitalis. These symptoms consisted in colored vision, chiefly white, green, yellow or red, flashes of light, positive colored scotomas, and other visual hallucinations. There was no change in the visual acuity or the usual fields of these patients, but the literature suggests that if the intoxication is sufficiently profound a temporary cortical type of blindness may result. This condition may occur in patients receiving

what is considered a normal dose of the drug and may be the only symptom present. Recovery takes place within two weeks after administration of the digitalis is stopped.

W S REESE

A CONTRIBUTION TO THE THEORY OF BINOCULAR VISION SUPPORTED BY THREE CASES OF LATENT NYSTAGMUS A POSNER, *Am J Ophth* 28:392 (April) 1945

Three cases of latent nystagmus with amblyopia of one eye are presented.

The nystagmus may be interpreted as a modification of normal fixation movements.

The nystagmus is inhibited by a minimal amount of binocular vision, which apparently brings into play a higher degree of cortical control than does monocular vision.

Observations made in these cases confirm the validity of Verhoeff's replacement theory of binocular vision.

The replacement theory also serves to explain the phenomenon of ocular dominance.

W S REESE

STUDIES IN DARK ADAPTATION AS A MEANS OF DETECTING DEFICIENCY OF VITAMIN A G W ROBERTSON and J YUDKIN, *Brit J Ophth* 28:556 (Nov) 1944

In this study, the instrument used was a modified and improved form of the adaptometer described by Hames (*Tr Ophth Soc U Kingdom* 48:103, 1938). In the measurements of final rod threshold, groups of 3 or 4 subjects each enter a dark room directly from their work, without any previous light adaptation. After the subjects have been in the dark for thirty-five or forty minutes, the dark adaptation of each subject is measured by noting the minimal amount of light which can just be seen. The 3 or 4 subjects in each group are tested in turn and then tested a second time in the same order. The second value is taken as the measure of dark-adapting capacity. The following summary is made. Measurements of dark adaptation may be used to assess nutritional level with respect to vitamin A either by determination of the effects of the vitamin on dark adaptation or by comparison of the values for dark adaptation in various groups. The latter method, while not providing such conclusive evidence as the former, may sometimes give presumptive evidence of the relative nutritional status with respect to the vitamin, and for technical reasons it may be the only feasible procedure. Using the former method of measuring vitamin A lability, the authors showed that deficiency of vitamin A existed in a small group of laboratory workers and in a large group of Birmingham (England) factory workers. Of these workers, 147 who took vitamin supplements showed a statistically significant improvement in dark adaptation, while

188 controls showed no significant change. Three groups of school children showed no sign of vitamin A deficiency with this method.

By comparison of the values for dark adaptation in various other groups, it was shown that the Birmingham factory workers and a group of Sheffield factory workers had significantly poorer dark adaptation than the three groups of school children whose dark adaptation had been shown to be unaffected by vitamin A.

W ZENTMAYER

### Vitreous

RUPTURE OF CHOROID ASSOCIATED WITH CYST OF VITREOUS. E ROSEN, *Brit J Ophth* 29 486 (Sept) 1945

The patient was a Negro aged 21 years. A batted ball struck the summit of the cornea of the right eye apparently directly, as the cornea was abraded. Two months after the injury there was a break in the sphincter of the iris with a segment of atrophy of the iris stroma. There was a choroidal tear in the macular region, and over its center was a biconvex band, the terminals of which were frayed out in a semicircular astral radiation. About 6 disk diameters below the disk was a peculiar cystic structure two and a half times the size of the disk and shaped like an apple. This sphere was loosely suspended from a pedicle and floated on movements of the globe, disclosing a phenomenon of variation in color from yellow to pink. The cyst would settle into a pocket formed by a proliferated connective tissue mass. Examination one month later showed that the cyst had ruptured.

The article is illustrated. W ZENTMAYER

### Therapeutics

PENICILLIN IN OPHTHALMOLOGY. ARNOLD SORSBY, *Brit M J* 2: 542 (Oct 20) 1945

Sorsby, on introducing the subject of penicillin therapy at a meeting of the section of ophthalmology of the Royal Society of Medicine, on Oct 11, 1945, stated that penicillin, as far as the eye was concerned, could not be regarded as a nontoxic substance or as a readily diffusible one. The absence of agreement among observers is partly due to the fact that samples of penicillin available at the moment were largely impure. He stated that it is possible to give penicillin in daily subconjunctival injections if the total dose is not more than 500 or 600 Oxford units. A constant corneal bath produced considerable penetration, and higher concentrations could be reached in the aqueous if ionization was

also used, but the combined method was difficult in practice. It has not been found possible experimentally to obtain an adequate concentration of penicillin in the anterior chamber with the use of ointment. If a massive dose was used slight penetration was obtained, but the difficulty with all these procedures was to obtain an adequate concentration in the eye. With subconjunctival injections a considerable concentration could be reached in the aqueous and vitreous, the drawback was the rapid excretion. After three hours hardly any penicillin was left in the anterior chamber, and, although the excretion was less rapid in the vitreous, the vitreous was extremely intolerant to injections of any type, and the author would not inject more than 200 or 300 units.

There is now a voluminous literature on the local uses of penicillin. The author mentioned 123 cases of ophthalmia neonatorum in which the drug was used during the last year. With a dose of 500 units per cubic centimeter, treatment was successful in 3 of 8 cases, with 1,000 units, in 4 of 7 cases, with 1,500 units, in 5 of 9 cases, and with 2,500 units, in 78 of 98 cases, with relapse in 13 cases and failures in 7 cases. Penicillin used locally was effective over the whole range of micro-organisms occurring with ophthalmia neonatorum. Frequency as well as concentration was important. When penicillin was applied at intervals of one hour, the results were good, at intervals of one-half hour they were better, and at intervals of five minutes, better still. For technical reasons it was not possible to institute the constant drip, and the author and his associates were instilling penicillin at intervals of one minute, and in most cases the condition was under control within half an hour.

Penicillin had been used in a number of ocular conditions. Good control of hypopyon ulcer was obtained with penicillin drops. Trachoma is a condition for which one would not expect the drug to be effective, since it is a virus infection. Sorsby had tried penicillin in 3 cases of trachoma, but only 1 was a fresh case, in this a good result was obtained. In cases of iridocyclitis the results so far reported in the literature have not been significant. The author had used penicillin in 1 case of sympathetic ophthalmia, with no very encouraging result.

The author feels that in penicillin one has a powerful agent but a limited one. It does not readily penetrate into the eye. Its extreme value is in local application for external infections. Unlike the sulfonamide compounds, it is not inactivated by pus, but in treatment of intraocular inflammation neither the sulfonamides nor penicillin has been helpful.

• ARNOLD KNAPP

# Society Transactions

EDITED BY DR W L BENEDICT

## NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

THOMAS H JOHNSON, M D, *Chairman*

WENDELL L HUGHES, M D, *Secretary*

*Regular Meeting, May 21, 1945*

### Ocular Sporotrichosis DR DAN M GORDON, Detroit

The tenth case of ocular sporotrichosis to be reported in the United States was presented. The patient came to the eye clinic of the New York Hospital with an "ulcerated" area on her left upper eyelid. This was followed by the development of a chain of subcutaneous nodules and associated lymphangitis. Cultures on Sabouraud's medium yielded a rich growth of the *Sporotrichum schenckii*. The patient was placed under oral treatment with potassium iodide and recovered. Pronouncement of cure was based on disappearance of the lesions and a sterile culture.

#### DISCUSSION

DR GEORGE M LEWIS (by invitation), In most cases of sporotrichosis, as Dr Gordon mentioned, a finger or hand is first affected, and then the lesions extend proximally up the arm, along the lymphatic chain. The initial lesion is often granulomatous and pus producing and may be confused with primary syphilis or pyoderma. When the second lesion appears, the diagnosis of sporotrichosis is not so difficult. In the laboratory diagnosis of this disease one will fail to demonstrate the organism if dependence is placed on stained smears or wet preparations. The diagnosis of sporotrichosis, unlike that of actinomycosis, is made from culture. The organism is seldom demonstrable in the stained preparation or the wet specimen. In Dr Gordon's case the diagnosis was easily made from culture once the condition was considered, but it is apparent that a certain degree of clinical acuity was needed even for consideration of sporotrichosis in this location.

The rare involvement of the eyelids is of interest. In cases of nail polish dermatitis the eyelids and the side of the neck are the favorite sites. The frequent contact of the hands with the face and the greater sensitivity of the eyelids than other portions of the face account for this occurrence. There may be an analogy between sensitization dermatitis and fungous infection, nevertheless, it seems logical that secondary autoinoculation is more frequently responsible for involvement of the eyelids with this infection.

Dr Gordon's slides illustrated a case of sporotrichosis appearing at the base of the thumb, with secondary lesions occurring along the lymphatic chain, and another case with involvement of the left lower eyelid and the left cheek. The infection in the second case was acquired by contact while the patient was caring for her daughter, who had the conventional type of sporotrichosis on the arm.

The organism has a typical appearance in culture on dextrose agar. The color is brown to black, and the surface configuration is constant. The growth itself has a pasty consistency and is well circumscribed. To verify the diagnosis, a hanging drop is made from the culture, and pyriform spores are noted in groups on the ends of small lateral branches.

As Dr Gordon stated, the treatment is usually simple, and satisfactory results may confidently be expected. Potassium iodide should be prescribed in increasing doses. The use of roentgen radiation may sometimes be considered. An occasional patient is intolerant to iodides, and sulfadiazine may then be substituted.

DR A RUSSELL SHERMAN, Newark, N J. I should like to ask Dr Gordon whether there is a relation between this condition and infection with *Streptothrix* or *Leptothrix*. Do these conditions resemble each other?

DR FRANK A VESEY. I should like to ask Dr Gordon whether any evidence of relative immunity has been established, or whether this condition is equally infectious to every one.

DR DAN M GORDON, Detroit. Infection with *Streptothrix* is usually seen in the conjunctival sac. I believe the only resemblance between *Sporothrix* and this fungus is the "ix" at the end of the name; the organisms are entirely different. *Streptotrichosis* is much more common; I saw a great deal of it in Chicago. The *leptothrix* is the organism found in Parinaud's conjunctivitis.

The question of immunity is an interesting one. I do not believe a single case of the disease in the American Indian has ever been reported. Two investigators have done considerable dermatologic work among the Indians. There was a case of the disease in a half-breed Indian. One case of sporotrichosis was reported by the Harvard expedition to Africa in 1937 or thereabouts; there may have been others, but in a paper published in 1943 only 1 African case was recorded.

I thought some one would ask about the mechanism of iodide therapy. Iodides are not specific in that they destroy the organism, but

they produce a fibroblastic reaction which walls off the organism. Loes stated that before he recognized sporotrichosis he saw a case of a condition which in retrospect he thought was sporotrichosis and which he diagnosed at the time as syphilis. The patient died in two months.

### Complications Incident to Simple Intracapsular Extraction. Procedures Designed Toward Prevention. DR. FRANK BRACKEN

This paper is published in full in this issue of the ARCHIVES, page 430

### Precisional Errors in Measurement of Squint and Phoria. MR. OTTO A. PUTNAM and DR. J. V. D. QUEREAU, Reading, Pa.

This paper was published in full in the July issue of the ARCHIVES, page 7

### DISCUSSION

DR. LEGRAND H. HARDY. Several important factors, present singly or in combination, may lead the incautious ophthalmologist into error in measuring squint and heterophoria with prisms.

1. The label on the prism. Most prisms bear a number, but to what unit this number refers is rarely stated. It may refer to the prism diopter ( $\Delta$ ), the centrad ( $\nabla$ ), the deviation produced at the position of minimal deviation or the apex angle of the prism. The unit is usually assumed to be the prism diopter. However, precise measurements carried out on this assumption over a period of several years on more than twenty sets of prisms showed that many of them were inaccurately labeled, the error at times reaching over 100 per cent. The most serious errors arose when the label referring to the apex angle, in degrees, was mistakenly assumed to refer to the power, in prism diopters.

2. The position in which the prism is held before the eye. The effect depends on the distance from the eye at which the prism is held and its angular rotation about one or more of three axes.

(a) A 40  $\Delta$  prism can accurately correct a 40  $\Delta$  deviation of the eye only under two conditions: first, when the fixation object is at infinity, and, second, when the effective surface of the prism is at the center of rotation of the eye. Since in measurement of a deviation for near vision the first condition must be violated and in practice the second condition can never be achieved, it follows that a 40  $\Delta$  prism can never neutralize 40  $\Delta$  of deviation in making a near point test. This is analogous to the change in effectivity of corrective lenses when placed in front of the eye. The effectivity of a lens will vary with change of its distance from the principal point of the eye.

When one considers the measurement of the deviation of a single eye, it is immediately ob-

vious that the relationship can be expressed thus

$$D = d + e$$

where  $D$  is the power of the prism,  $d$  is the deviation of the eye from the primary position and  $e$  is the angle, determined by two factors: (1) the proximity of the fixation point to the eye and (2) the distance at which the prism is held from the eye. The closer the fixation point is to the eye, the greater will be the angle  $e$ ; likewise, the greater the distance between the prism and the center of rotation of the eye, the greater will be the angle  $e$ .

A simple calculation for a single eye shows that if the deviation,  $d$ , is 30° (57.7  $\Delta$ ) and the fixation distance is 10 inches (25 cm) the prism necessary to correct this deviation will be 66.4  $\Delta$  if held 1 inch (2.5 cm) in front of the eye, or 83  $\Delta$  if held 3 inches (7.5 cm) in front of the eye.

When one considers two eyes which alternately fixate a near object, a new factor is introduced. Since the deviation is now measured not from the position of parallelism of the optic axes but from the lines joining the centers of rotations with the fixation point, this new factor will require a reorientation of the prism in convergent and divergent deviations. As one keeps the fixation object in the near field but moves it into the secondary positions of gaze, one introduces more complicating factors, which may disturb analyses unless properly evaluated. It is rare to see the fixation distance carefully maintained in these investigations involving the secondary positions of gaze, and even rarer to see the Prentice position of the prism and its effectivity distance maintained.

Aside from the marked change in effectivity brought about by changing the distance between the eye and the prism, other important positional factors operate.

(b) Rotation about the optic axis changes the effect of the prism from base in (or base out) to base up (or base down).

When strong prisms are used, this is an important factor to guard against.

(c) Rotation about a frontal horizontal axis from the base horizontal position produces complicated spatial distortion. The optical effects of this type of rotation have been analyzed by Southall.

(d) Rotation about a vertical axis from the base horizontal position produces little known but marked changes in power. The use of the term "prism diopter," involving, as it does, the fundamental postulate of Prentice (all power at one surface), introduces serious dangers. It is a valuable and convenient concept to use in prescribing therapeutic prisms to be incorporated in lenses, and its utility is conveniently and safely carried into the field of weak measuring prisms, but when powers above 20  $\Delta$  are utilized the danger of producing large errors



increases rapidly. A change of almost  $20\Delta$  can be effected by wrongly positioning a  $1\Delta$  prism. Such an effect probably never occurs since it would require almost  $80^\circ$  of rotation of the prism. However, with a  $30\Delta$  prism only  $22^\circ$  of rotation is required to increase its effective power to  $87\Delta$ , with a  $40\Delta$  prism a rotation of  $20^\circ$  will increase its effective power to  $97\Delta$ , and with a  $50\Delta$  prism a rotation of only  $8.5^\circ$  is needed to increase its effective power to almost  $104\Delta$ .

From these considerations, some practical rules may be formulated

1 In making near point measurements the prism should be held as close as possible to the eye. This reduces the effectivity factor

2 The use of a 16 or a 13 inch (40 or 33 cm) testing distance results in less error, owing to change in effectivity, than the use of a 10 inch (25 cm) testing distance. This advantage must be evaluated against the concomitant reduction in accommodation

3 A squint of over  $40\Delta$  should never be measured with prisms unless the power is split, approximately half being held before each eye. The error introduced by the inadvertent  $10^\circ$  rotation of two  $20\Delta$  prisms amounts to  $2 \times 2.75$ , or  $5.5\Delta$ , whereas the error introduced by the same amount ( $10^\circ$ ) of rotation of one  $40\Delta$  prism amounts to  $17.5\Delta$ . (It should be noted that use of the term "prism diopter" is invalid for any position except the Prentice)

4 In holding prisms before an eye, it is always safer to err by approaching the position of minimal deviation than by turning away from it. Such a maneuver has two advantages: (1) For a given rotation much less power effect is produced, and (2) the effect produced serves to detract from the effectivity factor rather than add to it. Thus, two errors tend to compensate for each other rather than to summate.

This discussion has considered only a few of the most elementary problems involved. Carrying these considerations into measurements involving the secondary positions of gaze has been part of the analytic work which Dr. Quereau and Mr. Putnam have imposed on themselves. I congratulate them and hope they will continue.

DR. JAMES WATSON WHITE. Dr. Quereau and Mr. Putnam have brought up two important points. It is important in making a diagnosis to get the proportionate differences, not only for distance and near vision but in the various directions of gaze. Whether the error is 3 or 5 prism degrees makes no difference in the diagnosis, as I see it, because the same variance from the true value is carried with a moderate degree of accuracy for distance and for near vision in the cardinal positions and would make no difference in diagnosis or in treatment.

I am afraid that Dr. Hardy's lucid description will scare off many people who do not understand this problem. I believe that if research men would work out these problems in the laboratory and tell the ophthalmologists what to do, and how, more progress would be made and more practical work done.

DR. JOSEPH I. PASCAL. The presentation of Dr. Quereau and Mr. Putnam was very instructive. Persons interested in this work will not find the mathematics hard to follow. But I want to ask Dr. Hardy a question about his objections to the prism diopter as a unit for prism measurement. Since the error introduced is due primarily to the prism not being held properly, that is, with the outer surface vertical, what difference would it make if the Jackson method of minimum deviation were used and the prism not held properly? If the prism is held the way Prentice intended it to be held, there is no error. If a prism made on the angle of minimum deviation is not held properly, that is, in the required position, which is symmetrically inclined to patient and examiner, would not similar errors be introduced?

DR. LEGRAND H. HARDY. The answer to Dr. Pascal's question is "no." The position from which a rotational error deviates is not a matter of indifference. From the graph of power plotted against angle of incidence, it is quite clear that the Prentice position of holding occupies a point on the curve at which errors of rotation of slight degree may cause pronounced changes in power. This is not true of the position of minimal deviation. The "split position" lies between the two. For example, a  $40\Delta$  prism exhibits  $40\Delta$  of effect in the Prentice position. If the angle of incidence is rotated  $10^\circ$  toward the apex, this power effect will reach  $57\Delta$ . The same prism shows  $32\Delta$  of power in the position of minimal deviation (if, for the sake of comparison, one is permitted to use the term "prism diopters" for any position except the Prentice). Rotating the prism  $10^\circ$  toward the apex from the position of minimal deviation will change its effective power from  $32$  to  $33\Delta$ . Fortunately, most ophthalmologists do not use the Prentice position of holding. They naively hold the prism in what I have called the "split position," which is nearer the position of minimal deviation than the Prentice position. In the "split position" a  $40\Delta$  prism exerts a comparative power of  $32.6\Delta$ , and a rotation of  $10^\circ$  toward the apex from the position changes the comparative power to about  $36\Delta$ . This should make it perfectly clear that in using high-powered metric (measuring) prisms the Prentice position is to be avoided, and, I believe, it constitutes a rational explanation of why one almost instinctively avoids the Prentice position, in spite of the fact that one may not, legitimately, use the term "prism diopters" for any but the Prentice position. For the incorpora-



tion of therapeutic prisms (up to  $8\Delta$ ) into lenses small departures from the Prentice position are unimportant, and the ease of using the Prentice method of calculating and numbering prisms justifies its application. For strong metric prisms used in measuring squint these statements do not remain valid.

Dr White's perturbation should be relieved by the four very practical rules I formulated in the opening discussion.

#### Aqueous Fibrin Fixation of Corneal Transplants in the Rabbit

DR HERBERT M KATZIN

This paper will be published in full in a future issue of the ARCHIVES.

#### Efficiency of the Lens: A Clinical Concept

DR JOSEPH I PASCAL

The effective power of a plus or minus correcting lens is changed when the lens is moved farther from or nearer the eye. This is known as change in effectivity. Another feature of change in the power of the lens not dependent on movement may be called lens efficiency. The inevitable separation of the correcting lens from the principal plane of the eye imparts to the convex lens positive efficiency because the correcting lens is always less than the true hypermetropic error it corrects in the principal plane of the eye. Conversely, the concave lens has negative efficiency because the concave correcting lens is always more than the true amount of myopia it corrects. Thus, a patient whose error is corrected with a  $-30.00$  D lens has a true myopia of only about  $20.00$  D.

A similar gradation of efficiency may be postulated with respect to the accommodation. Whereas the person with natural emmetropia accommodates  $1.00$  D for every diopter of distance, the person with corrected ametropia accommodates either more or less than  $1.00$  D for every diopter of distance. If the accommodation of the natural emmetrope is considered as normal efficiency, the lens of the person with corrected hypermetropia has negative efficiency and the lens of the person with corrected myopia has positive efficiency. The reason is that the person with corrected hypermetropia always has to accommodate more than the dioptric value of the object distance, while the person with corrected myopia has to accommodate less than the dioptric value of the object distance.

Fundamentally, this difference in accommodative efficiency is due to the fact that each person with corrected ametropia has what may be considered his own basic accommodative unit. While the accommodative unit of the natural emmetrope is  $1.00$  D, the accommodative unit of the person with corrected hypermetropia is always more than  $1.00$  D and that of the person with corrected myopia is always less than  $1.00$  D. Thus,

the accommodative unit of the person with corrected hypermetropia of  $5.00$  D is  $1.23$  D and that of the person with corrected myopia of  $5.00$  D is only  $0.83$  D (calculation based on  $20$  mm as the distance of the lens from the principal plane of the eye).

For a dioptric distance of  $4.00$  D ( $0.25$  meter) the natural emmetrope accommodates  $4.00$  D, the person with corrected hypermetropia of  $5.00$  D accommodates four times his basic unit, which amounts to  $4.92$  D, and the person with corrected myopia of  $5.00$  D accommodates four times his basic unit, which amounts to only  $3.32$  D. Because of the different accommodative units, the person with corrected myopia becomes presbyopic later than the person with corrected hypermetropia. For the same reason, the same near point of accommodation shows more true accommodative power in the subject with corrected hypermetropia than in the subject with corrected myopia.

In the presbyopic correction of anisometropia, the same addition can never place both eyes in focus for any near distance. The more hypermetropic eye, like the less myopic eye, needs a stronger addition to compensate for the different accommodative units. This difference in units also leads to a variability of astigmatic errors for near distance.

The lens which replaces the accommodation also has positive or negative efficiency, depending on whether its power is less or more, respectively, than the accommodation it replaces. The lens which replaces the accommodation in the person with natural emmetropia has negative efficiency, it is always a little more than the accommodation it replaces, and it increases in power according as it replaces the first, second, third or fourth diopter of accommodation. Thus, it takes a  $+1.02$  D lens to replace the first diopter of accommodation, a  $+1.06$  D lens to replace the second diopter, a  $+1.11$  D lens to replace the third diopter, a  $+1.16$  D lens to replace the fourth diopter, and so on. The replacing lens for corrected hypermetropia has positive efficiency as long as it replaces part or all of the accommodation that can be used to neutralize the hypermetropia. Thereafter it has negative efficiency. The replacing lens in corrected myopia always has negative efficiency.

Another feature of lens efficiency concerns the form of the correcting lens. Lenses of different form all of which have the same vertex power have the same efficiency for distant, but not for near, vision. For near vision, the double convex lens has the greatest efficiency, the meniscus convex, the least efficiency.

#### DISCUSSION

DR ARTHUR LINKSZ, Hanover, N. H. Any one who is interested in refined refraction must be enthusiastic about Dr Pascal's presentation. Within the last few years Dr Hughes and Dr

Sugar have published papers in which they showed that there are cases in which the axis of astigmatism for near vision may be different from that for distance. About a year ago Dr Pascal himself added to knowledge in this field, demonstrating that the effectivity of an astigmatic correction is, for intrinsic reasons, different for near and for distant vision. In work on aniseikonia I have been confronted in many cases with the fact that the aniseikonic correction for near vision may be different from the one for distance. All these data remind one that a good deal of basic research is still necessary to refine refraction for close work, and especially the method of addition in close work for presbyopic persons. As Dr Pascal has just shown, this is not as simple as it is usually thought to be.

One point needs especial emphasis. Dr Pascal has given a new fundamental concept in what he calls the "accommodative unit." This is a concept with which we all as ophthalmologists will have to become thoroughly familiar. We may hope that much eyestrain, distress and difficulty will be avoided in the future by prescribing corrections for near work in terms of accommodative units and accommodative efficiency rather than in terms of the rigid system which has so far been used.

DR JOSEPH I. PASCAL: This work is not difficult and can be simplified if one takes the concept of the basic accommodative unit. Each refractive condition, after being corrected, has its own basic accommodative unit. In cases of anisometropia, when the eyes accommodate for any distance — 1 or 2 D — the difference between the accommodation of the two eyes will be the difference between their accommodative units and the multiples thereof. The same applies to astigmatism, in which each principal meridian has its own accommodative unit. In general, this concept of a basic accommodative unit clarifies, I think, many things which seemed difficult before.

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### CORRECTION

In the report of the American Ophthalmological Society in the August issue (*ARCH OPHTH* 34:163, 1945) the following remarks were omitted from the discussion on the paper by Dr Algernon Reese, entitled "Deep Chamber Glaucoma Due to Formation of a Cuticular Product in the Filtration Angle," (bottom of the first column, continuing the discussions by Dr Verhoeft):

That bullous keratitis and the related condition, pannus degenerativus, occur in many of the eyes such as Dr Reese has described is of no significance in regard to the character of the original changes in the ligament but does indicate that the glaucoma was in an advanced stage and had damaged the corneal endothelium.

Therefore, while the occurrence of bullous keratitis suggests that alteration of the endothelium led to the formation of elastic membrane in the angle, it also suggests that this formation occurred after the glaucoma had been long established.

If, as Dr Reese asserts, the conditions that lead to the formation of membrane over the ligament are the same as those that exist in cases of epithelial dystrophy, one would expect that glaucoma would be a frequent complication of this disorder. This, however, is certainly not the case. Also, since warts on Descemet's membrane are commonly found at the periphery of senile eyes, one would expect on the basis of Dr Reese's views that glaucoma would occur far more frequently in senile eyes than it actually does.

In spite of everything I have said, I am convinced that in Dr Reese's cases the glaucoma was produced by the changes he describes. I reconcile his observation with mine by assuming that in his cases a tendency to endothelial proliferation existed and that this finally caused obstruction to outflow, and by assuming that in my cases the tendency did not exist but that the changes over the ligament, including the less extensive formation of elastic membrane, resulted from the glaucoma. In other words, I think that Dr Reese has made a remarkable and highly important discovery.

DR FREDERICK A. DAVIS, Madison, Wis.: I have had a case recently which may belong to the group described by Dr Reese.

The patient, a married woman aged 63, was first seen ten weeks ago. She complained of acute pain and loss of vision in her right eye. The pain was excruciating and was accompanied with nausea and vomiting. She had not noticed any reduction in vision prior to this attack, which occurred two weeks before she consulted me. Local treatment and administration of sedatives by her family physician had brought slight relief, but vision had grown progressively worse. Examination revealed a moderately inflamed globe. The cornea was steamy, having a ground-glass appearance. The anterior chamber was deep. The aqueous appeared to be clear and was free of cells so far as could be determined with the slit lamp. No keratic precipitates were present. The pupil was dilated and fixed, measuring 4 to 5 mm. No definite synechias could be seen, the iris was atrophic. Tension was 59 mm in the right eye and 17 mm in the left eye, with the Schiøtz tonometer. Vision was 20/70 in the right eye and 20/20 in the left eye.

A whitish mass of some foreign substance was present in the temporal and inferior region of the chamber angle. It appeared to be fused with the cornea. It did not present the ordinary characteristics of an inflammatory exudate, nor did it appear to be a new growth.

The fundus could be seen indistinctly, but there appeared to be moderate temporal cupping of the disk. Gonioscopic studies were not made because of the corneal haze and inflammation.

The patient was treated intensively in the hospital for nineteen days with miotics and hot applications.

The acute inflammatory symptoms subsided somewhat, and the tension was reduced to 37 mm. Schiøtz. An Elliott trephine operation was performed by my assistant, Dr. P. A. Duehr, with very satisfactory results. The tension fell to 17 mm., the corneal edema disappeared, and the eye gradually became quiet. Study of the fundus revealed typical glaucomatous cupping of the disk. The field of vision showed concentric contraction to about 20 degrees. The pupil has remained semidilated and fixed at 5 mm. No synechias can be seen. The iris is atrophic. Vision is now 20/50.

The left eye is apparently unaffected, fields, fundus and tension being normal.

The patient is still under observation, and further studies of the chamber angle will be carried out.

DR ALGERNON REESE, New York. Dr. Kronfeld points out the importance which central vision and visual fields would have been in establishing whether or not these patients came to enucleation early or whether or not the cases on which this report is based was cases of far advanced glaucoma. The corneal changes were so extensive that central vision or the visual fields would not be an accurate criterion. Also, the corneal changes prevented an accurate view of the interior of the eye.

Dr. Verhoeff points out that this type of glaucoma should be more prevalent in older people. The average age in these cases was only 50 years. He also states that glaucoma should be more prevalent in cases of cornea guttata. I agree with him in both these contentions.

Furthermore, one would expect glaucoma due to this process to be present in both eyes.

I believe the case which Dr. Davis cites belongs to this group. Dr. Friedenwald poses the question whether glaucoma with an abnormally deep anterior chamber is due to this type of lesion in all cases. In my series, 26 cases were thought to belong to this group, but there were 16 additional cases of deep chamber glaucoma with open angle which did not belong here.

I very much appreciate the discussion, and I think Dr. Verhoeff has been particularly generous.

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## Correspondence

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### REQUEST FOR COPIES OF THE ARCHIVES OF OPHTHALMOLOGY FOR OPHTHALMOLOGISTS ABROAD

*To the Editor*—Since 1941 American publications have not been available to most of the Continental centers and investigators. I have had several letters from ophthalmologists abroad indicating the desire and need for ophthalmic literature which has appeared during these war years.

It occurred to me that some subscribers of the ARCHIVES with copies for the past several years would be willing to send their copies abroad to ophthalmic centers or to individuals. If such subscribers will write to the Howe Library of Ophthalmology, c/o Miss Jeanette Loessel, 243 Charles Street, Boston 14, a name and address will be provided to which the ARCHIVES may be sent. Arrangements are being made to reimburse the donors for the cost of mailing.

DAVID G. COGAN, M.D., Boston  
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President Dr Gordon B New, Mayo Clinic, Rochester,  
Minn  
President-Elect Dr Alan C Woods, Johns Hopkins  
Hospital, Baltimore 5  
Executive Secretary-Treasurer Dr William L Bene-  
dict, 100-1st Ave Bldg, Rochester, Minn

## AMERICAN OPHTHALMOLOGICAL SOCIETY

President Dr S Judd Beach, 704 Congress St, Port-  
land, Maine  
Secretary-Treasurer Dr Walter S Atkinson, 129  
Clinton St, Watertown, N Y

## ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC

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CANADIAN MEDICAL ASSOCIATION, SECTION ON  
OPHTHALMOLOGY

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St, Toronto  
Secretary-Treasurer Dr L J Sebert, 170 St George  
St, Toronto

CANADIAN OPHTHALMOLOGICAL SOCIETY

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Toronto 5  
Secretary-Treasurer Dr Kenneth B Johnston, Suite 1,  
1509 Sherbrooke St W, Montreal

NATIONAL SOCIETY FOR THE PREVENTION OF  
BLINDNESS

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Secretary Miss Regina E Schneider, 1790 Broadway,  
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SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY,  
SECTION ON EYE, EAR NOSE AND THROAT

President Dr N Zwaifler, 46 Wilbur Ave, Newark  
Secretary Dr William F Keim Jr, 25 Roseville Ave,  
Newark  
Place 91 Lincoln Park South, Newark Time 8 45  
p m, second Monday of each month, October to May

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr Watson Gailey, 1000 N Main St,  
Bloomington, Ill  
Secretary-Treasurer Dr William F Hubble, 861-867  
Citizens Bldg, Decatur, Ill

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr L J Friend, 425 E Grand Ave, Beloit,  
Wis  
Secretary Dr G L McCormick, 626 S Central Ave,  
Marshfield

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President Dr Theodore L Terry, 140 Marlborough St,  
Boston  
Secretary-Treasurer Dr Merrill J King, 264 Beacon  
St, Boston  
Place Massachusetts Eye and Ear Infirmary, 243  
Charles St, Boston Time 8 p m, thrd Tuesday of  
each month from November to April, inclusive

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President Dr D H O'Rourke, 1612 Tremont Pl,  
Denver  
Secretary-Treasurer Dr C Allen Dickey, 450 Sutter  
St, San Francisco

PUGET SOUND ACADEMY OF OPHTHALMOLOGY  
AND OTO-LARYNGOLOGY

President Dr James H Mathews, 1317 Marion St,  
Seattle, Wash  
Secretary-Treasurer Dr Barton E Peden, 301 Stimson  
Bldg, Seattle 1  
Place Seattle or Tacoma, Wash Time Thrd Tues-  
day of each month except June, July and August

ROCK RIVER VALLEY EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr J Sheldon Clark, 27 E Stephenson St,  
Freeport, Ill  
Secretary-Treasurer Dr Harry R Warner, 321 W  
State St, Rockford, Ill  
Place Rockford, Ill, or Janesville or Beloit, Wis  
Time Thrd Tuesday of each month from October  
to April, inclusive

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr L D Gomon, 308 Eddy Bldg, Saginaw,  
Mich  
Secretary-Treasurer Dr Harold H Heuser, 207  
Davidson Bldg, Bay City, Mich  
Place Saginaw or Bay City, Mich Time Second  
Tuesday of each month, except July, August and  
September

SIOUX VALLEY EYE AND EAR ACADEMY

President Dr J C Decker, 515 Francis Bldg, Sioux  
City, Iowa  
Secretary-Treasurer Dr J E Dvorak, 408 Davidson  
Bldg, Sioux City, Iowa

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE,  
EAR, NOSE AND THROAT

Chairman Dr John H Burleson, 414 Navarro St,  
San Antonio, Texas  
Secretary Dr J W Jervey Jr, 101 Church St,  
Greenville, S C

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE  
AND THROAT

President Dr H L Brehmer, 221 W Central Ave,  
Albuquerque, N Mex  
Secretary Dr A E Cruthrds, 1011 Professional Bldg,  
Phoenix, Ariz

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President Dr W M Dodge, 716 First National Bank  
Bldg, Battle Creek  
Secretary-Treasurer Dr Kenneth Lowe, 25 W Mich-  
igan Ave, Battle Creek  
Time Last Thursday of September, October, Novem-  
ber, March, April and May

WESTERN PENNSYLVANIA EYE, EAR, NOSE and  
THROAT SOCIETY

President Dr Ray Parker, 218 Franklin St, Johns-  
town, Pa  
Secretary-Treasurer Dr J McClure, Tyson, Deposit  
Nat'l Bank Bldg, Dubois

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR,  
NOSE AND THROAT SECTION

President Dr Raymond C Cook, 701 Main St, Little  
Rock  
Secretary Dr K W Cosgrove, Urquhart Bldg, Little  
Rock



## COLORADO OPHTHALMOLOGICAL SOCIETY

President Dr C A Ringle, 912-9th Ave, Greeley  
 Secretary Dr W A Ohmart, 1102 Republic Bldg,  
 Denver  
 Place University Club, Denver Time 7 30 p m,  
 third Saturday of each month, October to May, in-  
 clusive

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON  
EYE, EAR, NOSE AND THROAT

President Dr F L Phillips, 405 Temple St, New  
 Haven  
 Secretary-Treasurer Dr W H Turnley, 1 Atlantic  
 St, Stamford, Conn

## EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President Dr William O Martin Jr, Doctors Bldg,  
 Atlanta  
 Secretary-Treasurer Dr C K McLaughlin, 526  
 Walton St, Macon

INDIANA ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr F McK Ruby, Union City  
 Secretary Dr Edwin W Dyar Jr, 23 E Ohio St,  
 Indianapolis  
 Place French Lick Time First Wednesday in April

IOWA ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr J K Von Lackum, 117-3d St S E,  
 Cedar Rapids  
 Secretary-Treasurer Dr B M Merkel, 604 Locust St,  
 Des Moines

KANSAS STATE MEDICAL SOCIETY, SECTION ON OPH-  
THALMOLOGY AND OTOLARYNGOLOGY

President Dr W D Pittman, Pratt  
 Secretary Dr Louis R Haas, 902 N Broadway,  
 Pittsburg

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND  
OTOLARYNGOLOGICAL SOCIETY

President Dr Val H Fuchs, 200 Carondelet St, New  
 Orleans  
 Secretary-Treasurer Dr Edley H Jones, 1301 Wash-  
 ington St, Vicksburg, Miss

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA,  
SECTION ON EYE, EAR, NOSE AND THROAT  
DISEASES

Chairman Dr Karl M Houser, 2035 Delancey St,  
 Philadelphia 3  
 Secretary Dr William T Hunt Jr, 1205 Spruce St,  
 Philadelphia 7

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF  
OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr Edmond L Cooper, 1543 Woodward  
 Ave, Detroit 26  
 Secretary Dr Ralph H Gilbert, 110 Fulton St E,  
 Grand Rapids

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr Karl C Wold, 1051 Lowry Bldg, St  
 Paul 2  
 Secretary Dr William A Kennedy, 372 St Peter St,  
 St Paul 2  
 Time Second Friday of each month from October to  
 May

## MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President Dr William Morrison, 208 N Broadway,  
 Billings  
 Secretary Dr Fritz D Hurd, 309 Medical Arts Bldg,  
 Great Falls

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr W Howard Morrison, 1500 Medical  
 Arts Bldg, Omaha  
 Secretary-Treasurer Dr John Peterson, 1307 N St,  
 Lincoln

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON  
OPHTHALMOLOGY, OTOLOGY AND  
RHINOLARYNGOLOGY

Chairman Dr George P Meyer, 410 Haddon Ave,  
 Camden  
 Secretary Dr John P Brennan, 429 Cooper St,  
 Camden

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR,  
NOSE AND THROAT SECTION

Chairman Dr Harold J Joy, 504 State Tower Bldg,  
 Syracuse 2  
 Secretary Dr Maxwell D Ryan, 660 Madison Ave,  
 New York 21

NORTH CAROLINA EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr Hugh C Wolfe, 102 N Elm St,  
 Greensboro  
 Secretary Dr Vanderbilt F Couch, 104 W 4th St,  
 Winston-Salem

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY  
AND OTO-LARYNGOLOGY

President Dr W L Diven, City National Bank Bldg,  
 Bismarck  
 Secretary-Treasurer Dr A E Spear, 20 W Villard,  
 Dickinson

OREGON ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr Paul Neely, 1020 S W Taylor St,  
 Portland  
 Secretary-Treasurer Dr Lewis Jordon, 1020 S W  
 Taylor St, Portland  
 Place Good Samaritan Hospital, Portland Time  
 Third Tuesday of each month

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr Lewis T Buckman, 83 S Franklin St,  
 Wilkes-Barre  
 Secretary Pro Tem Dr Paul C Craig, 232 N 5th  
 St, Reading  
 Time Last week in April

RHODE ISLAND OPHTHALMOLOGICAL AND  
OTOLOGICAL SOCIETY

Acting President Dr N Darrell Harvey, 112 Water-  
 man St, Providence  
 Secretary-Treasurer Dr Linley C Happ, 124 Water-  
 man St, Providence  
 Place Rhode Island Medical Society, Library, Provi-  
 dence Time 8 30 p m, second Thursday in  
 October, December, February and April

**SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY**

President Dr J L Sanders, 222 N Main St, Greenville  
Secretary Dr J H Stokes, 125 W Cheves St, Florence

**TENNESSEE ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY**

President Dr Wesley Wilkerson, 700 Church St, Nashville  
Secretary-Treasurer Dr W D Stinson, 124 Physicians and Surgeons Bldg, Memphis

**TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL  
SOCIETY**

President Dr F H Rosebrough, 603 Navarro St, San Antonio  
Secretary Dr M K McCullough, 1717 Pacific Ave, Dallas

**UTAH OPHTHALMOLOGICAL SOCIETY**

President Dr E B Fairbanks, 315 Medical Arts Bldg, Salt Lake City  
Secretary-Treasurer Dr Dean Spear, 516 Boston Bldg, Salt Lake City  
Place University Club, Salt Lake City Time 7 00 p m, third Monday of each month

**VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND  
OPHTHALMOLOGY**

President Dr Mortimer H Williams, 30½ Franklin Rd S W, Roanoke  
Secretary-Treasurer Dr Meade Edmunds, 34 Franklin St, Petersburg

**WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE,  
EAR, NOSE AND THROAT SECTION**

President Dr George Traugh, 309 Cleveland Ave, Fairmont  
Secretary Dr Welch England, 621½ Market St, Parkersburg

**LOCAL**

**AKRON ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY**

President Dr E L Mather, 39 S Main St, Akron, Ohio  
Secretary-Treasurer Dr V C Malloy, 2d National Bank Bldg, Akron, Ohio  
Time First Monday in January, March, May and November

**ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY**

President Dr B M Cline, 153 Peachtree St N E, Atlanta, Ga  
Acting Secretary Dr A V Hallum, 478 Peachtree St N E, Atlanta, Ga  
Place Grady Hospital Time 6 00 p m, fourth Monday of each month, from October to May

**BALTIMORE MEDICAL SOCIETY, SECTION ON  
OPHTHALMOLOGY**

Chairman Dr Ernst Bodenheimer, 1212 Eutaw Pl, Baltimore  
Secretary Dr Thomas R O'Rourke, 104 W Madison St, Baltimore  
Place Medical and Chirurgical Faculty, 1211 Cathedral St Time 8 30 p m, fourth Thursday of each month from October to March

**BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB**

President Each member, in alphabetical order  
Secretary Dr Luther E Wilson, 919 Woodward Bldg, Birmingham, Ala  
Place Tutwiler Hotel Time 6 30 p m, second Tuesday of each month, September to May, inclusive

**BROOKLYN OPHTHALMOLOGICAL SOCIETY**

President Dr Michael J Buonaguro, 589 Lorimer St, Brooklyn 11  
Secretary-Treasurer Dr Louis Freemark, 256 Rochester Ave, Brooklyn 13  
Place Kings County Medical Society Bldg, 1313 Bedford Ave Time Third Thursday in February, April, May, October and December

**BUFFALO OPHTHALMOLOGIC CLUB**

President Dr William H Howard, 389 Linwood Ave, Buffalo 9  
Secretary-Treasurer Dr Sheldon B Freeman, 196 Linwood Ave, Buffalo 9  
Time Second Thursday of each month from October to May

**CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY**

President Each member, in alphabetical order  
Secretary Dr Douglas Chamberlain, Chattanooga Bank Bldg, Chattanooga, Tenn  
Place Mountain City Club Time Second Thursday of each month from September to May

**CHICAGO OPHTHALMOLOGICAL SOCIETY**

President Dr Samuel J Meyer, 58 E Washington St, Chicago 2  
Secretary Dr W A Mann, 30 N Michigan Ave, Chicago 2  
Place Continental Hotel, 505 N Michigan Ave  
Time Third Monday of each month from October to May

**CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY  
STAFF**

Chairman Dr D T Vail, 441 Vine St, Cincinnati  
Secretary Dr A A Levin, 441 Vine St, Cincinnati  
Place Cincinnati General Hospital Time 7 45 p m, third Friday of each month except June, July and August

**CLEVELAND OPHTHALMOLOGICAL CLUB**

Chairman Dr M Paul Motto, Rose Bldg, Cleveland  
Secretary Dr H H Wygand, Guardian Bldg, Cleveland  
Time Second Tuesday in October, December, February and April

**COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION  
ON OPHTHALMOLOGY**

Chairman Dr W S Reese, 1901 Walnut St, Philadelphia  
Clerk Dr George F J Kelly, 37 S 20th St, Philadelphia  
Time Third Thursday of every month from October to April, inclusive

## COLUMBUS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

Chairman Dr Erwin W Troutman, 21 E State St, Columbus, Ohio  
 Secretary-Treasurer Dr T Rees Williams, 380 E Town St, Columbus 15, Ohio  
 Place University Club Time 6 15 p m, first Monday of each month, from October to May, inclusive

## CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr C B Collins, 704 Medical Professional Bldg, Corpus Christi, Texas  
 Secretary Dr L W O Janssen, 710 Medical Professional Bldg, Corpus Christi, Texas  
 Time 6 30 p m, third Tuesday of each month from October to May

## DALLAS ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Ruby K Daniel, Medical Arts Bldg, Dallas 1, Texas  
 Secretary Dr Tom Barr, Medical Arts Bldg, Dallas 1, Texas  
 Place Dallas Athletic Club Time 6 30 p m, first Tuesday of each month from October to June The November, January and March meetings are devoted to clinical work

## DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr H C Schmitz, 604 Locust St, Des Moines, Iowa  
 Secretary-Treasurer Dr Byron M Merkel, 604 Locust St, Des Moines, Iowa  
 Time 7 45 p m, third Monday of every month from September to May

## DETROIT OPHTHALMOLOGICAL CLUB

Chairman Members rotate alphabetically  
 Secretary Dr Wesley G Reid, 667 Fisher Bldg, Detroit 2  
 Place Club rooms of Wayne County Medical Society  
 Time First Monday of each month, November to April, inclusive

## DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Raymond S Goux, 545 David Whitney Bldg, Detroit 26  
 Secretary Dr Arthur Hale, 1609 Eaton, Tower, Detroit 26  
 Place Club rooms of Wayne County Medical Society  
 Time 6 30 p m, third Thursday of each month from November to April, inclusive

## EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President Appointed at each meeting  
 Secretary-Treasurer Dr Joseph L Holohan, 330 State St, Albany  
 Time Third Wednesday in October, November, March, April, May and June

## FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Rex Howard, 602 W 10th St, Fort Worth, Texas  
 Secretary-Treasurer Dr R H Gough, Medical Arts Bldg, Fort Worth, Texas  
 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each month except July and August

## HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SECTION

President Dr Lyle J Logue, 1304 Walker Ave, Houston, Texas  
 Secretary Dr John T Stough, 803 Medical Arts Bldg, Houston, Texas  
 Place Medical Arts Bldg, Harris County Medical Society Rooms Time 8 p m, second Thursday of each month from September to June

## INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr Myron Harding, 23 E Ohio St, Indianapolis  
 Secretary Dr Kenneth L Craft, 23 E Ohio St, Indianapolis  
 Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each month from November to May

## KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo  
 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo  
 Time Third Thursday of each month from October to June The November, January and March meetings are devoted to clinical work

## LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Francis Carl Hertzog, 117 E 8th St, Long Beach, Calif  
 Secretary-Treasurer Dr Robert G Thornburgh, 117 E 8th St, Long Beach, Calif  
 Place Seaside Hospital Time Last Wednesday of each month from October to May

## LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Orrie E Ghrist, 210 N Central Ave, Glendale, Calif  
 Secretary-Treasurer Dr K C Brandenburg, 110 Pine Ave, Long Beach 2, Calif  
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time 6 30 p m, fourth Monday of each month from September to May, inclusive

## LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky  
 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky  
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

LOWER ANTHRACITE EYE, EAR, NOSE AND  
THROAT SOCIETY

Chairman Each member in alphabetical order  
Secretary Dr James J Monohan, 31 S Jardin St,  
Shenandoah, Pa

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA,  
SECTION OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

Chairman Dr P S Constantinople, 1835 I St N. W.,  
Washington  
Secretary Dr Frazier Williams, 1801 I St N W,  
Washington  
Place 1718 M St N W Time 8 p m, third Friday  
of each month from October to April, inclusive

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

Chairman Each member, in alphabetical order  
Secretary Dr Sam H Sanders, 1089 Madison Ave,  
Memphis, Tenn  
Place Eye Clinic of Memphis Eye, Ear, Nose and  
Throat Hospital Time 8 p m, second Tuesday of  
each month from September to May

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Ralph T Rank, 238 W Wisconsin Ave,  
Milwaukee  
Secretary-Treasurer Dr Frank G Treskow, 411 E  
Mason St, Milwaukee 2  
Place University Club Time 6 30 p m, fourth  
Tuesday of each month from October to May

MONTREAL OPHTHALMOLOGICAL SOCIETY

Chairman Dr H V Dutrow, 1040 Fidelity Medical  
Bldg, Dayton, Ohio  
Secretary-Treasurer Dr Maitland D Place, 981 Rei-  
bold Bldg, Dayton, Ohio  
Place Van Cleve Hotel Time 6 30 p m, first Tues-  
day of each month from October to June, inclusive

MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr J Rosenbaum, 1396 Ste Catherine St  
W, Montreal, Canada  
Secretary Dr L Tessier, 1230 St Joseph Blvd E,  
Montreal, Canada  
Time Second Thursday of October, December, Febru-  
ary and April

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

Chairman Dr M M Cullom, 700 Church St, Nash-  
ville, Tenn.  
Secretary Dr R. E Sullivan, 432 Doctors Bldg,  
Nashville, Tenn  
Place James Robertson Hotel Time 6 30 p m, third  
Monday of each month from October to May

NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President Dr William H Ryder, 185 Church St,  
New Haven, Conn  
Secretary Dr Frederick A Wiess, 255 Bradley St,  
New Haven, Conn

NEW ORLEANS OPHTHALMOLOGICAL AND OTO-  
LARYNGOLOGICAL SOCIETY

President Dr W B Clark, 1012 American Bank Bldg,  
New Orleans  
Secretary Dr Mercer G Lynch, 1018 Maison Blanche  
Bldg, New Orleans  
Place Louisiana State University Medical Bldg  
Time 8 p m, second Tuesday of each month from  
October to May

NEW YORK ACADEMY OF MEDICINE, SECTION OF  
OPHTHALMOLOGY

Chairman Dr Rudolf Aebli, 30 E 40th St, New York  
Secretary Dr Truman L Boyes, 654 Madison Ave,  
New York  
Time 8 30 p m, third Monday of every month from  
October to May, inclusive

NEW YORK SOCIETY FOR CLINICAL  
OPHTHALMOLOGY

President Dr Maurice L Wieselthier, 1322 Union St,  
Brooklyn  
Secretary Dr Benjamin Esterman, 983 Park Ave,  
New York 28  
Place New York Academy of Medicine, 2 E 103d St  
Time 8 p m, first Monday of each month from  
October to May, inclusive

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr James P Luton, 117 N Broadway,  
Oklahoma City  
Secretary Dr Harvey O Randel, 117 N Broadway,  
Oklahoma City  
Place University Hospital Time Second Tuesday of  
each month from September to May

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL  
AND OTO-LARYNGOLOGICAL SOCIETY

President Dr A A Steinberg, 1502 Farnam St, Omaha  
Secretary-Treasurer Dr W Howard Morrison, 1500  
Medical Arts Bldg, Omaha 2  
Place Omaha Club, 20th and Douglas Sts, Omaha  
Time 6 p m dinner, 7 p m program, third Wednes-  
day of each month from October to May

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President Dr Thomas Sanfacon, 340 Park Ave,  
Paterson, N J  
Secretary-Treasurer Dr J Averbach, 435 Clinton  
Ave, Clinton, N J  
Place Paterson Eye and Ear Infirmary Time 9 p m,  
last Friday of every month, except June, July and  
August

PHILADELPHIA COUNTY MEDICAL SOCIETY,  
EYE SECTION

President Dr Isaac Tassman, 136 S 16th St, Phila-  
delphia  
Secretary Dr Glen Gregory Gibson, 255 S 17th St,  
Philadelphia  
Time First Thursday of each month from October  
to May

## PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President Dr Clarence F Bernatz, Park Bldg, Pittsburgh  
 Secretary Dr Robert J Billings, Park Bldg, Pittsburgh  
 Place Pittsburgh Academy of Medicine Bldg Time  
 Fourth Monday of each month, except June, July  
 August and September

## READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Isaac B High, 326 N 5th St, Reading, Pa  
 Secretary Dr Paul C Craig, 232 N 5th St, Reading Pa  
 Place Wyomissing Club Time 6 30 p m, third  
 Wednesday of each month from September to July

## RICHMOND EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Luther C Brawner, Professional Bldg, Richmond, Va  
 Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va  
 Place Westmoreland Club Time 6 p m, second  
 Monday of each month from October to May

## ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y  
 Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

## ST LOUIS OPHTHALMIC SOCIETY

President Dr Vincent Jones, 634 N Grand Blvd, St Louis  
 Secretary Dr T E Sanders, 508 N Grand Blvd, St Louis 3  
 Place Oscar Johnson Institute Time Fourth Friday  
 of each month from October to April, inclusive,  
 except December, at 8 00 p m

## SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President Dr Belvin Pritchett, 705 E Houston St, San Antonio 5, Texas  
 Secretary-Treasurer Lt Col John L Matthews, AAF  
 School of Aviation Medicine, Randolph Field, Texas  
 Place San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center  
 Time 7 p m, second Tuesday of each month from  
 October to May

SAN FRANCISCO COUNTY MEDICAL SOCIETY,  
SECTION ON EYE, EAR, NOSE AND THROAT

Chairman Dr Roy H Parkinson, 870 Market St, San Francisco  
 Secretary Dr A G Rawlins, 384 Post St, San Francisco  
 Place Society's Bldg, 2180 Washington St, San Francisco  
 Time Fourth Tuesday of every month except  
 June, July and December

## SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President Dr David C Swearingen, Slattery Bldg, Shreveport, La  
 Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La  
 Place Shreveport Charity Hospital Time 7 30 p m,  
 first Monday of every month except July, August  
 and September

## SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Clarence A Veasey Sr, 421 W Riverside Ave, Spokane, Wash  
 Secretary Dr Clarence A Veasey, 421 W Riverside Ave, Spokane, Wash  
 Place Spokane Medical Library Time 8 p m, fourth  
 Tuesday of each month except June, July and August

## SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President Dr A H Rubenstein, 713 E Genesee St, Syracuse, N Y  
 Secretary-Treasurer Dr I H Blaisdell, 713 E Genesee St, Syracuse, N Y  
 Place University Club Time First Tuesday of each  
 month except June, July and August

## TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr L C Ravin, 316 Michigan St, Toledo 2, Ohio  
 Secretary Dr W W Randolph, 1838 Parkwood Ave, Toledo, Ohio  
 Place Toledo Club Time Each month except June,  
 July and August

## TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

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